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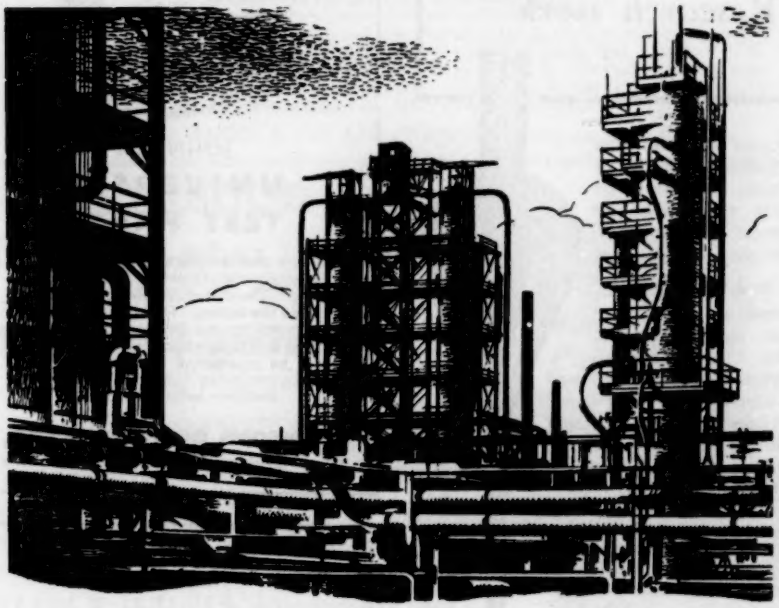

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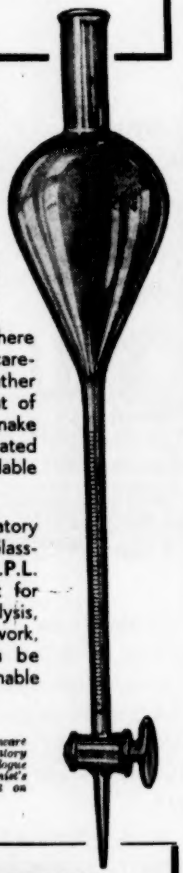

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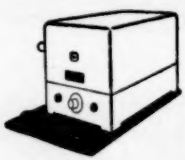

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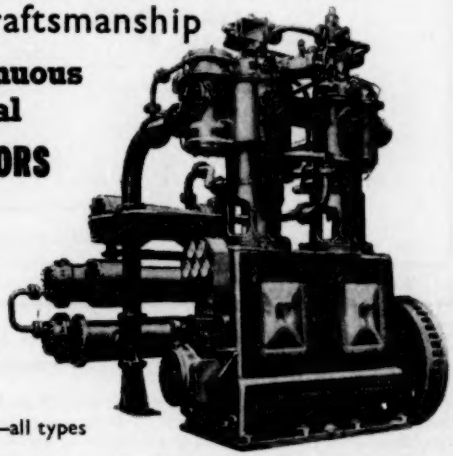

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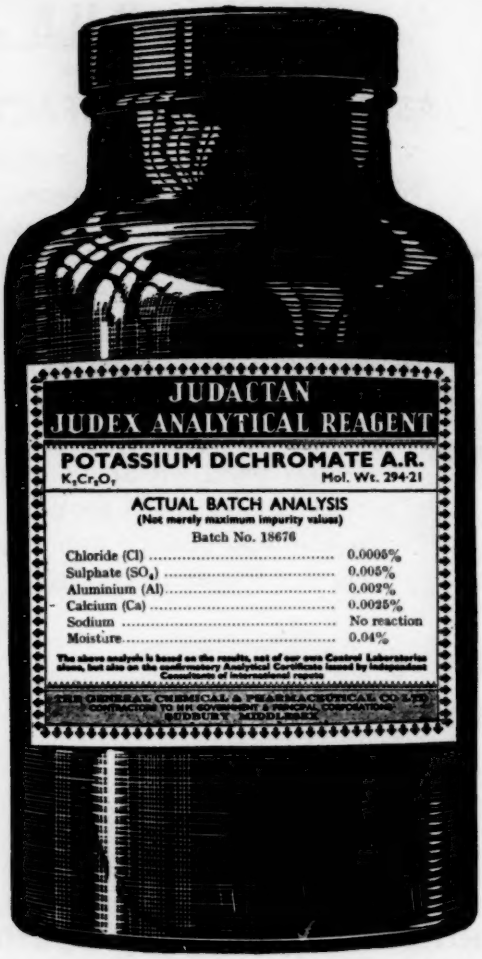
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3. Communications which have appeared or have been accepted for publication with essentially the same scientific content in another Journal or freely available printed work shall not be published in the *Journal* of the Society unless this course is approved by the Council.

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SUMMARY. 9. Every paper must be prefaced by a short summary (50—250 words) setting forth briefly and in simple language the objects of the investigation and the results obtained. The summary should give any chemist a clear idea of what the investigation has achieved and should be independent of the main text. "Notes" do not require a summary.

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ILLUSTRATIONS. 13. Illustrations accompanying the papers must be carefully drawn, preferably *twice* the size of the finished block (max. width 5 inches), *in Indian ink, on good white cartridge paper* (graph paper with faint blue lines is acceptable). Any illustration which seriously exceeds four times the size of the finished block will be returned to the author for re-drawing to a smaller scale. Lettering on the drawings, whether on the margin or in the body of the drawing, must not be in ink but must be inserted *clearly but lightly in pencil*. *Margins* of at least two inches must be left. Authors may, if they wish, submit in the first place clearly drawn pencil sketches instead of the completed diagrams, which, however, must be supplied before publication. Further information can be obtained from the Editor.

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INTERNATIONAL ATOMIC WEIGHTS, 1949.

[Reprinted from 15th Report of the Commission on Atomic Weights of the International Union of Pure and Applied Chemistry.]

	Symbol.	Atomic number.	Atomic weight.*
Actinium	Ac	89	227
Aluminium	Al	13	26·97
Americium	Am	95	[241]
Antimony	Sb	51	121·76
Argon	A	18	39·944
Arsenic	As	33	74·91
Astatine	At	85	[210]
Barium	Ba	56	137·36
Beryllium	Be	4	9·013
Bismuth	Bi	83	209·00
Boron	B	5	10·82
Bromine	Br	35	79·916
Cadmium	Cd	48	112·41
Calcium	Ca	20	40·08
Carbon	C	6	12·010
Cerium	Ce	58	140·13
Cæsium	Cs	55	132·91
Chlorine	Cl	17	35·457
Chromium	Cr	24	52·01
Cobalt	Co	27	58·94
Copper	Cu	29	63·54
Curium	Cm	96	[242]
Dysprosium	Dy	66	162·46
Erbium	Er	68	167·2
Europium	Eu	63	152·0
Fluorine	F	9	19·00
Francium	Fr	87	[223]
Gadolinium	Gd	64	156·9
Gallium	Ga	31	69·72
Germanium	Ge	32	72·60
Gold	Au	79	197·2
Hafnium	Hf	72	178·6
Helium	He	2	4·003
Holmium	Ho	67	164·94
Hydrogen	H	1	1·0080
Indium	In	49	114·76
Iodine	I	53	126·92
Iridium	Ir	77	193·1
Iron	Fe	26	55·85
Krypton	Kr	36	83·7
Lanthanum	La	57	138·92
Lead	Pb	82	207·21
Lithium	Li	3	6·940
Lutetium	Lu	71	174·99
Magnesium	Mg	12	24·32
Manganese	Mn	25	54·93
Mercury	Hg	80	200·61
Molybdenum	Mo	42	95·95
Neodymium	Nd	60	144·27
Neptunium	Np	93	[237]
Neon	Ne	10	20·183
Nickel	Ni	28	58·69
Niobium	Nb	41	92·91
Nitrogen	N	7	14·008
Osmium	Os	76	190·2
Oxygen	O	8	16·0000
Palladium	Pd	46	106·7
Phosphorus	P	15	30·98
Platinum	Pt	78	195·23
Plutonium	Pu	94	[239]
Polonium	Po	84	210
Potassium	K	19	39·096
Praseodymium	Pr	59	140·92
Promethium	Pm	61	[147]
Protactinium	Pa	91	231
Radium	Ra	88	226·05
Radon	Rn	86	222
Rhenium	Re	75	186·31
Rhodium	Rh	45	102·91
Rubidium	Rb	37	85·48
Ruthenium	Ru	44	101·7
Samarium	Sm	62	150·43
Scandium	Sc	21	45·10
Selenium	Se	34	78·96
Silicon	Si	14	28·06
Silver	Ag	47	107·880
Sodium	Na	11	22·997
Strontium	Sr	38	87·63
Sulphur	S	16	32·066
Tantalum	Ta	73	180·88
Technetium	Tc	43	[99]
Tellurium	Te	52	127·61
Terbium	Tb	65	159·2
Thallium	Tl	81	204·39
Thorium	Th	90	232·12
Thulium	Tm	69	169·4
Tin	Sn	50	118·70
Titanium	Ti	22	47·90
Tungsten	W	74	183·92
Uranium	U	92	238·07
Vanadium	V	23	50·95
Xenon	Xe	54	131·3
Ytterbium	Yb	70	173·04
Yttrium	Y	39	88·92
Zinc	Zn	30	65·38
Zirconium	Zr	40	91·22

* A value given in brackets denotes the mass number of the most stable known isotope.

[The names given above are those adopted by the Chemical Society.]

INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY.
AMSTERDAM, 1949.

THE Commission on Nomenclature of Inorganic Chemistry made the following recommendations which were adopted by the Council of the International Union :

1. *The names of elements which have been recently discovered or synthesised.*

The following names are recommended, subject to such modifications as may be necessary in other languages :

Atomic number.	Name.
43	Technetium
61	Promethium
85	Astatine
87	Francium
93	Neptunium
94	Plutonium
95	Americium
96	Curium

2. *The names to be applied to certain elements for which two or more names are current.*

The following are recommended :

Atomic number.	Name.
4	Beryllium
41	Niobium
71	Lutetium
72	Hafnium
74	Wolfram *
92	Protactinium

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* Tungsten (and not wolfram) will nevertheless be used in all publications of the Chemical Society.

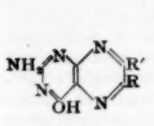
JOURNAL
OF
THE CHEMICAL SOCIETY

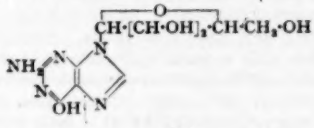
1. *Synthesis of 8-Substituted Pteridine Derivatives.*

By H. S. Forrest, R. Hull, H. J. Rodda, and A. R. Todd.

Structural relationships between the natural pteridines, the purine nucleosides, and the flavins suggest that pteridine derivatives bearing a carbohydrate residue attached to $N_{(8)}$ might be expected to occur in Nature. Methods for the synthesis of such compounds have been investigated and the preparation of 5 : 6 : 7 : 8-tetrahydro-6-keto-2 : 4-dimethyl-8-phenylpteridine, 8-ethyl-leucopterin, 4-amino-8-D-glucosyl-5 : 6 : 7 : 8-tetrahydro-6 : 7-diketo-2-methylthiopteridine and some related substances is described.

Interest in the derivatives of pteridine has been stimulated in recent years by the discovery that they occur among the insect colouring matters (cf. Gates, *Chem. Reviews*, 1947, **41**, 63) and in the folic acid group of vitamins (cf. Simpson, *Ann. Reports.*, 1946, **43**, 250). A comparison of the naturally occurring pteridine structures (I) with the purine nucleoside guanosine (II) and the *iso*alloxazine riboflavin (III) shows a striking similarity between them in so far as the pyrimidine portion of their respective molecules is concerned. Formally, the guanosine molecule


(I.)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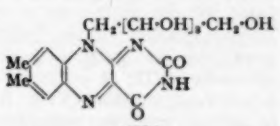
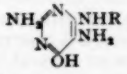

(III.)

might derive from a 2 : 5-diamino-6-hydroxy-4-D-ribosylaminopyrimidine (IV; R = D-ribosyl) by reaction with formic acid, and riboflavin from a closely related substance (IV; R = D-ribityl) by condensation with 3 : 4-dimethyl-*o*-benzoquinone and subsequent deamination. Although there is no evidence that this view has biogenetic significance, the fact that condensation of an intermediate (IV) with an open-chain α-diketone would yield a pteridine derivative bearing a carbohydrate side-chain on $N_{(8)}$, suggested an investigation into the synthesis of compounds of this type. No natural pteridine so far isolated bears a $N_{(8)}$-substituent, but on the above view the natural occurrence of, for example, an 8-*N*-glycoside is at least a possibility (cf. Shive *et al.*, *J. Amer. Chem. Soc.*, 1950, **72**, 2817; Elion *et al.*, *Arch. Biochem.*, 1950, **26**, 337), and in any case it would be of some interest to know whether such a compound would act as a biological antagonist to the purine nucleosides or the flavins.

To this end, investigations were begun on the synthesis of some model compounds in order to explore possible general methods of preparation. We first considered the synthesis of a $N_{(8)}$-phenyl compound starting from the known 5-amino-4-hydroxy-2 : 6-dimethylpyrimidine (V; R = OH, R′ = NH_2) (Andersag and Westphal, *Ber.*, 1937, **70**, 2044) which was prepared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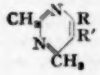
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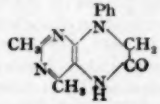
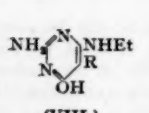

(VI.)

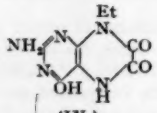
(VII.)

by catalytic, in preference to dithionite, reduction of 4-hydroxy-2 : 6-dimethyl-5-phenylpyrimidine. The above authors converted the aminopyrimidine into the corresponding chloro-

compound by heating it with phosphorus pentachloride and phosphoryl chloride, but the yield was not stated and in our hands the yields obtained were so low (*ca.* 14%) that various modifications were investigated. Chloroacetylation of the aminopyrimidine to give 5-chloroacetamido-4-hydroxy-2 : 6-dimethylpyrimidine (V; R = OH; R′ = NH·CO·CH_2Cl) followed by treatment of this with phosphoryl chloride likewise proved unsatisfactory. Reaction of 4-chloro-5-formamido-2 : 6-dimethylpyrimidine (V; R = Cl; R′ = NH·CHO; Hull, Lovell, Openshaw, and Todd, *J.*, 1947, 41) with aniline, however, followed by hydrolysis, yielded 5-amino-4-anilino-2 : 6-dimethylpyrimidine (V; R = NHPh; R′ = NH_2) which with chloroacetyl chloride was converted into 4-anilino-5-chloroacetamido-2 : 6-dimethylpyrimidine (V; R = NHPh; R′ = NH·CO·CH_2Cl). Cyclisation of this to 5 : 6 : 7 : 8-tetrahydro-6-keto-2 : 4-dimethyl-8-phenylpteridine (VI) was then effected in reasonable yield by using silver carbonate and silver acetate as in Purrmann's classical synthesis (*Annalen*, 1940, **546**, 98).

An 8-alkyl compound would clearly be a better model for an 8-glycoside than an 8-phenyl compound, however, and consequently a satisfactory synthesis of a 4-alkylamino-2-amino-6-hydroxypyrimidine was sought. Reaction of ethylamine with 2-amino-4-chloro-6-methoxypyrimidine (Gabriel and Colman, *Ber.*, 1903, **36**, 3381) caused disubstitution to give 2-amino-4 : 6-bisethylaminopyrimidine (VII; R = R″ = NHEt) and, with 2-amino-4 : 6-dichloropyrimidine under pressure it gave 2-amino-4-chloro-6-ethylaminopyrimidine (VII; R = NHEt; R′ = Cl). The last-mentioned compound was then converted by sodium methoxide into the 6-methoxypyrimidine (VII; R = NHEt; R′ = OMe) but hydrolysis of this to the hydroxy-compound


(VIII.)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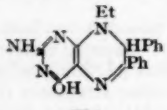
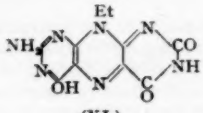
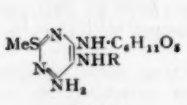
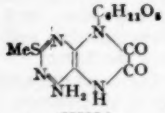
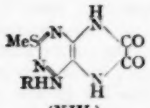

(X.)


(XI.)

under conditions analogous to those used by Hilbert and Johnson (*J. Amer. Chem. Soc.*, 1930, **52**, 4489) for the hydrolysis of the methoxy-group in 2-keto-6-methoxy-3-tetra-acetylglucosylaminopyrimidine proved troublesome and gave low yields. Finally, 2-amino-4 : 6-dichloropyrimidine was partially hydrolysed with sodium hydroxide to 2-amino-4-chloro-6-hydroxypyrimidine (VII; R = Cl; R′ = OH) and this gave a reasonable yield of 2-amino-4-ethylamino-6-hydroxypyrimidine (VII; R = NHEt; R′ = OH). Nitrosation of this proceeded readily in mineral acid, and reduction of the product (VIII; R = NO) by chemical (dithionite) or catalytic (Pd–$BaSO_4$ in sodium carbonate solution) means gave the amine (VIII; R = NH_2) which was not generally isolated since it was extremely sensitive to atmospheric oxidation. Treatment of the crude amine with chloroacetyl chloride gave 2-amino-5-chloroacetamido-4-ethylamino-6-hydroxypyrimidine (VIII; R = NH·CO·CH_2Cl), but all attempts to cyclise this to a ketopteridine were unsuccessful. However, treatment of (VIII; R = NH_2) with oxalic acid gave 8-ethyl-leucopterin (IX); with benzoin it gave 2-amino-7 : 8-dihydro-8-ethyl-4-hydroxy-6 : 7-diphenylpteridine (X) and, with alloxan, 7-amino-9-ethyl-2 : 3 : 4 : 9-tetrahydro-5-hydroxy-2 : 4-diketo-1 : 3 : 6 : 8 : 9 : 10-hexa-aza-anthracene (a diaza*iso*alloxazine) (XI).


(XII.)


(XIII.)


(XIV.)

Attention was next turned to the synthesis of a $N_{(8)}$-glycoside. The above model experiments had been carried out in anticipation of starting from a 2-amino-6-glycosylamino-4-hydroxypyrimidine, but so far the preparation of such a compound has not been found possible (Andrews, Anand, Todd, and Topham, *J.*, 1949, 2490), thus invalidating some of the cyclisation experience gained with the model compounds. However, 5 : 6-diamino-2-methylthio-4-D-tetra-acetylglucosylaminopyrimidine, prepared by a procedure slightly modified from that of Holland, Lythgoe, and Todd (*J.*, 1948, 965), reacted smoothly with chloroacetyl chloride to give 6-amino-5-chloroacetamido-2-methylthio-4-tetra-acetyl-D-glucosylaminopyrimidine (XII; R = CO·CH_2Cl) as its hydrochloride, but this again could not be cyclised to a pteridine. Again (XII; R = H) did not react with benzoin, and with alloxan appeared to give a complex mixture

of products, but in a modified Purrmann synthesis, with ethyl oxalate and sodium methoxide, it gave 4-amino-8-D-glucosylamino-5 : 6 : 7 : 8-tetrahydro-6 : 7-diketo-2-methylthiopteridine (XIII). It is obvious that there is an alternative route for ring formation in this compound, involving the free amino-group in position 6 of the pyrimidine ring to give (XIV), although, by analogy with the cyclisation of 4-glycosylamino-5-thioformamidopyrimidines to 9-glycosylpurines, it was expected that the 8-glycosylpteridine would be at least the major product.

Attempts to determine the structure of the reaction product by nitrous acid treatment were not successful for, in contrast to behaviour of the purines, it has been shown that a free amino-group in position 4 of the pteridine ring is resistant to such treatment (Taylor and Cain, *J. Amer. Chem. Soc.*, 1949, **71**, 2538) and more specifically by us that 4-aminopteridine is unaffected by nitrous acid. Similarly, the ready hydrolysis of the 4-amino-group (*idem*, *ibid.*) could not be used as a means of identification in this case because of the presence of the acid-sensitive glycosidic link. That the formulation given above is indeed correct was finally shown by periodate titrations. Thus, (XIV; R = glucosyl) would be expected to show an uptake of 5—6 moles of periodate (Howard, Kenner, Lythgoe, and Todd, *J.*, 1946, 861), including 1 mole for the oxidation of the methylthio-group (Howard, Lythgoe, and Todd, *J.*, 1945, 556), whereas (XIII) should take up not more than 3 moles. In fact, when the oxidation was carried out in 50% dimethylformamide at 0°, the compound showed an uptake of 2 moles in 48 hours, followed by a further slow uptake of 1 mole in 10 days, and at room temperature in aqueous suspension with constant shaking there was a fairly rapid (24 hours) uptake of 3 moles, after which oxidation ceased. Model experiments on 4-amino-5 : 6 : 7 : 8-tetrahydro-6 : 7-diketo-2-methylthiopteridine (XIV; R = H), prepared analogously from 4 : 5 : 6-triamino-2-methylthiopyrimidine, were complicated by extreme insolubility, but (XIV; R = H) was unaffected by periodate at 0° and showed a very slow uptake (0·33 mole in 7 days) at room temperature, thus indicating that the ring structure was not a complicating factor in the oxidation.

Experimental.

5-Amino-4-hydroxy-2 : 6-dimethylpyrimidine (V; R = OH; R′ = NH_2).—4-Hydroxy-2 : 6-dimethyl-5-phenylazopyrimidine (20 g.) and palladised barium sulphate (2 g.) were shaken in ethanol (250 c.c.) in the presence of hydrogen at atmospheric pressure. The theoretical quantity of hydrogen was absorbed during 3 hours. Filtration, evaporation of the filtrate under reduced pressure in a nitrogen atmosphere, and removal of aniline from the residue by washing it with acetone gave the product (10·5 g.), m. p. 196—197° (Andersag and Westphal, *loc. cit.*, give m. p. 194°).

5-Chloroacetamido-4-hydroxy-2 : 6-dimethylpyrimidine (V; R = OH; R′ = NH·CO·CH_2Cl).—Chloroacetyl chloride (2·14 c.c.) was added to a stirred solution of 5-amino-4-hydroxy-2 : 6-dimethylpyrimidine (3·57 g.) in acetone containing suspended potassium carbonate (1·57 g.). After 2 hours' stirring, the mixture was set aside overnight, whereafter the solid was collected and dried, and then extracted with methanol. The crude product obtained by evaporation of the extract was purified by vacuum-sublimation followed by recrystallisation from ethanol, giving the *amide* as small colourless needles, m. p. 216—217° (Found : C, 44·3; H, 4·9; N, 19·3. $C_8H_{10}O_2N_3Cl$ requires C, 44·5; H, 4·6; N, 19·4%).

Treatment of this product with phosphoryl chloride gave small amounts of 5-amino-4-chloro-2 : 6-dimethylpyrimidine and 5-amino-4-hydroxy-2 : 6-dimethylpyrimidine.

5-Amino-4-anilino-2 : 6-dimethylpyrimidine (V; R = NHPh; R′ = NH_2).—4-Chloro-5-formamido-2 : 6-dimethylpyrimidine (1·21 g.) and aniline (15 c.c.) were heated under reflux for 4 hours. Excess of aniline was removed by distillation, and the solid residue was dissolved in dilute hydrochloric acid, refluxed for 15 minutes, and then cooled and the solution made alkaline. The precipitated solid was collected, washed with cold water, and recrystallised from benzene from which the *product* separated in needles (1·45 g.), m. p. 192—193° (Found : C, 67·7; H, 6·4; N, 25·8. $C_{12}H_{14}N_4$ requires C, 67·3; H, 6·5; N, 26·2%). The same material was similarly prepared from 5-amino-4-chloro-2 : 6-dimethylpyrimidine.

4-Anilino-5-chloroacetamido-2 : 6-dimethylpyrimidine (V; R = NHPh; R′ = NH·CO·CH_2Cl).—Chloroacetyl chloride (0·285 c.c.) was added to a well stirred solution of 5-amino-4-anilino-2 : 6-dimethylpyrimidine (0·77 g.) in acetone containing suspended potassium carbonate (0·26 g.). Next morning, the solid (0·53 g.) was collected, washed with acetone and then water, and finally recrystallised from carbon tetrachloride, from which the *amide* separated in needles, m. p. 139—140° (Found : C, 57·3; H, 5·2; N, 19·6. $C_{14}H_{15}ON_4Cl$ requires C, 57·8; H, 5·2; N, 19·3%). Further small quantities (0·27 g.) were obtained by treating the acetone mother-liquors with more chloroacetyl chloride.

5 : 6 : 7 : 8-Tetrahydro-6-keto-2 : 4-dimethyl-8-phenylpteridine (VI).—The above chloroacetamido-compound (0·4 g.) was added to a solution of silver acetate (0·14 g.) in boiling water (30 c.c.), followed by silver carbonate (0·3 g.). After 2 hours' refluxing, the black residue was collected by centrifugation and extracted thrice with hydrochloric acid. Addition of excess sodium acetate to the extract precipitated the *pteridine* derivative, which, recrystallised from aqueous ethanol, had m. p. 262—264° (Found : C, 66·0; H, 5·7; N, 22·2. $C_{14}H_{14}ON_4$ requires C, 66·2; H, 5·5; N, 22·1%). Yield, 0·15 g. It was soluble in ethanol, aqueous acetic acid (50%), and aqueous sodium hydroxide, but insoluble in benzene and water.

2-*Amino*-4 : 6-*bisethylaminopyrimidine* (VII; R = R′ = NHEt).—2-Amino-4-chloro-6-methoxypyrimidine (Gabriel and Colman, *loc. cit.*) (2·8 g.) and ethylamine (30 c.c.; 30% w/v) were heated in an autoclave at 150° for 4 hours. Evaporation of the resulting yellow solution under reduced pressure gave an oily residue which was dissolved in dilute hydrochloric acid and precipitated as a solid (2·35 g.), m. p. 125—128°, by addition of excess of sodium hydroxide. The *product* was purified by vacuum-sublimation and recrystallised from benzene, forming feathery needles, m. p. 135·5—136° (Found : C, 53·1; H, 8·4; N, 38·9. $C_8H_{18}N_8$ requires C, 53·0; H, 8·3; N, 38·7%).

2-*Amino*-4-*chloro*-6-*ethylaminopyrimidine* (VII; R = NHEt; R′ = Cl).—2-Amino-4 : 6-dichloropyrimidine (5·0 g.) and ethylamine (8·3 c.c.; 33% w/v) diluted with water (10 c.c.) were heated in an autoclave at 100° for 3 hours. The product was collected from the cooled solution, dissolved in dilute hydrochloric acid, filtered to remove unchanged starting material, and then reprecipitated by addition of sodium hydroxide. Recrystallisation from aqueous ethanol gave prismatic needles of 2-*amino*-4-*chloro*-6-*ethylaminopyrimidine*, m. p. 152·5° (Found : C, 41·7; H, 5·1; N, 32·3. $C_6H_9N_4Cl$ requires C, 41·7; H, 5·2; N, 32·4%).

2-*Amino*-4-*ethylamino*-6-*methoxypyrimidine* (VII; R = NHEt; R′ = OMe).—The above chloro-compound (6·3 g.) in methanol (60 c.c.) was heated with methanolic sodium methoxide (from 1·01 g. of sodium in 15 c.c. of methanol) in an autoclave at 130° for 3 hours. Removal of solvent and crystallisation first from water (charcoal) and then benzene gave the *ether* (5·2 g.) as colourless needles, m. p. 137—138° (Found : C, 49·6; H, 6·9; N, 33·7. $C_7H_{12}ON_4$ requires C, 50·0; H, 7·1; N, 33·3%).

2-*Amino*-4-*ethylamino*-6-*hydroxypyrimidine* (VII; R = NHEt; R′ = OH).—(a) *From* 2-*amino*-4-*ethylamino*-6-*methoxypyrimidine*. Dry hydrogen chloride was passed into a solution of 2-amino-4-ethylamino-6-methoxypyrimidine (0·8 g.) in ethanol (20 c.c.), and the mixture heated under reflux during 3 hours. The syrup produced on evaporation was heated with ethanol (2 c.c.) and the whole set aside overnight. The colourless solid was stirred with excess of cold bicarbonate solution, and the residual solid was recrystallised from ethanol, forming colourless prisms, m. p. 229—230° (Found : C, 46·6; H, 6·1; N, 36·1. $C_6H_{10}ON_4$ requires C, 46·7; H, 6·5; N, 36·4%).

(b) *From* 2-*amino*-4 : 6-*dichloropyrimidine*. 2-Amino-4 : 6-dichloropyrimidine (10 g.) was refluxed with sodium hydroxide (122 c.c. of N.). After 4 hours, 2-*amino*-4-*chloro*-6-*hydroxypyrimidine* (7·9 g.) (VII; R = Cl; R′ = OH) was precipitated with acetic acid; it had m. p. 261° (Found : C, 33·3; H, 2·9; N, 28·6. $C_4H_4ON_3Cl$ requires C, 33·0; H, 2·8; N, 28·8%). This product and ethylamine (22 c.c.; 31% w/w from decomposition of its hydrochloride) were heated in a sealed tube at 120° for 4 hours. The solid obtained on cooling was dissolved in dilute hydrochloric acid (charcoal), reprecipitated with bicarbonate, and finally crystallised from ethanol, to give prisms, m. p. 227—228°, undepressed on admixture with material prepared by method (a) above.

2-*Amino*-4-*ethylamino*-6-*hydroxy*-5-*nitrosopyrimidine* (VIII; R = NO).—A solution of 2-amino-4-ethylamino-6-hydroxypyrimidine (5 g.) in dilute hydrochloric acid (35 c.c. of 3N. + 50 c.c. water) was cooled to 0° and treated with sodium nitrite (3·75 g.) in water (50 c.c.). The solution was set aside overnight at 0°, then neutralised with sodium carbonate, and the precipitated solid (4 g.) collected; a further quantity (1 g.) was obtained by evaporation of the mother-liquors. Recrystallisation from a large volume of water (4 g./l.) gave the *nitroso*-compound in yellow plates, changing to red-violet on storage or more rapidly on heating, m. p. 265—266° (decomp.) (Found, in material dried at 110° : C, 39·5; H, 5·0; N, 38·5. $C_6H_9O_2N_5$ requires C, 39·2; H, 4·9; N, 38·2%).

2 : 5-*Diamino*-4-*ethylamino*-6-*hydroxypyrimidine* (VIII; R = NH_2).—The above nitroso-compound (3·12 g.) was dissolved in water (50 c.c.) containing sodium hydroxide (4·25 g.) and sodium dithionite (11·2 g.) added during 10 minutes at 60—70°, a vigorous stream of nitrogen being passed through the mixture during the operation. The colour of the solution changed to yellow and a yellow solid was deposited. The mixture was cooled and the pH adjusted to 9·0—9·5; the yellow crystalline 6-*hydroxy*-compound (2·12 g.) was collected, washed with water, and dried, and then had m. p. 236—237° (Found : N, 40·5. $C_6H_{11}ON_5$ requires N, 41·4%). Further purification could not be effected, as the compound decomposed rapidly by oxidation during all attempts at recrystallisation.

2-*Amino*-5-*chloroacetamido*-4-*ethylamino*-6-*hydroxypyrimidine* (VIII; R = NH·CO·CH_2Cl).—2 : 5-Diamino-4-ethylamino-6-hydroxypyrimidine (3·4 g.) in water (250 c.c.) containing sodium hydroxide (1·6 g.) was shaken vigorously with a solution of chloroacetyl chloride (3 c.c.) in light petroleum (100 c.c.; b. p. 40—60°) for 15 minutes with cooling. A cream-coloured solid was deposited and this was collected and washed with water. Recrystallisation from water or methanol gave fine white needles (3·8 g.), m. p. 213—214°, of the *chloroacetamide* (Found, in material dried at 100° : C, 38·8; H, 5·0. $C_8H_{12}O_2N_5Cl$ requires C, 39·1; H, 4·9%).

8-*Ethyl*-*leucopterin* (IX).—2 : 5-Diamino-4-ethylamino-6-hydroxypyrimidine (1·5 g.; freshly prepared) was ground intimately with oxalic acid (8·9 g.), and the mixture (under slight vacuum) was heated in an oil-bath. At 120—140°, the mass fused and water was evolved; when this evolution ceased (30 minutes), the temperature was raised to 260° for 15 minutes. The cooled mass was then extracted with warm water (150 c.c.), and the residual solid dissolved in sodium hydroxide solution (150 c.c. of 0·1N.). The solution was boiled with charcoal and filtered into a boiling solution of dilute hydrochloric acid (150 c.c. of 0·1N.). On cooling, a brownish-yellow microcrystalline powder was deposited. Repetition of this procedure gave 8-*ethyl*-*leucopterin* as a yellow-brown microcrystalline solid (Found, in material dried at 140° : C, 43·5; H, 4·0; N, 30·9. $C_8H_9O_3N_5$ requires C, 43·1; H, 4·0; N, 31·5%).

2-*Amino*-8-*ethyl*-7 : 8-*dihydro*-4-*hydroxy*-6 : 7-*diphenylpteridine* (X).—The above freshly prepared diamino-compound (0·5 g.) and benzoin (0·8 g.) were refluxed in a mixture of ethanol (5 c.c.) and acetic acid (3 c.c.) for 2 hours. Cooling caused the deposition of yellow crystals (0·7 g.) which were collected; the mother-liquors, poured into water, gave a further quantity of yellow solid (0·4 g.) which was combined with the above crystals. The crude product was purified by dissolution in hot sodium hydroxide

solution and filtration into excess of dilute acetic acid. The *diphenylpteridine* was obtained as yellow needles on recrystallisation from aqueous pyridine (30%) (Found : C, 69·5; H, 5·5; N, 20·3. $C_{26}H_{18}ON_4$ requires C, 69·6; H, 5·5; N, 20·3%). It was insoluble in water but slightly soluble in ethanol or acetic acid.

7-Amino-9-ethyl-2 : 3 : 4 : 9-tetrahydro-5-hydroxy-2 : 4-diketo-1 : 3 : 6 : 8 : 9 : 10-hexa-aza-anthracene (XI).—The nitroso-compound (0·5 g.) was hydrogenated in sodium carbonate solution (10 c.c.; saturated) with palladised barium sulphate and, after filtration and evaporation to dryness *in vacuo*, the residue was dissolved in a mixture of glacial acetic acid (5 c.c.) and ethanol (10 c.c.); alloxan (0·5 g.) was added and the whole was refluxed for 2 hours. The solution was then evaporated to dryness and the residue triturated with water and collected (0·8 g.). It was then dissolved in boiling sodium hydroxide (10 c.c. of 2N.), and the solution filtered and then acidified to pH 5 with acetic acid. The yellow microcrystalline *product* was collected and recrystallised from aqueous pyridine or water, from which it tended to separate in semi-colloidal form (Found, in material dried at 150°/0·1 mm. : C, 44·3; H, 3·3; N, 34·9. $C_{10}H_8O_3N_7$ requires C, 43·6; H, 3·3; N, 35·6%).

6-Amino-2-methylthio-5-nitroso-4-tetra-acetyl-D-glucosidaminopyrimidine.—6-Amino-4-D-glucosylamino-2-methylthio-5-nitrosopyrimidine (2·58 g.) (Holland, Lythgoe, and Todd, *loc. cit.*) was kept at room temperature for 36 hours with acetic anhydride (5·4 c.c.) in pyridine (50 c.c.). Ethanol (25 c.c.) was then added (temperature, <10°) and after 2 hours the solution was evaporated to dryness under reduced pressure. Ice-water was added and the green product (3·45 g.) was collected and washed with water. It was purified by passing its solution in ethyl acetate through a column of neutral alumina. Evaporation of the main eluate gave the *nitroso*-compound as blue needles, m. p. 154° (Found : C, 44·1; H, 4·8; N, 13·9. $C_{19}H_{25}O_{10}N_5S$ requires C, 44·3; H, 4·8; N, 13·6%).

5 : 6-Diamino-2-methylthio-4-tetra-acetyl-D-glucosylaminopyrimidine.—Zinc dust (10 g.) was added to a solution of the above nitroso-compound (5 g.) in boiling ethanol (150 c.c.) containing glacial acetic acid (5 c.c.) and heating was continued for 10 minutes. Filtered and cooled, the solution deposited a yellowish solid (3·7 g.) which was collected and washed with ice-water to remove inorganic material. Two recrystallisations from ethanol gave the diamine as pale yellow needles, m. p. 214° (Found, in material dried at 110° : C, 45·4; H, 5·5; N, 13·9. Calc. for $C_{19}H_{27}O_9N_5S$: C, 45·5; H, 5·4; N, 14·0%).

6-Amino-5-chloroacetamido-2-methylthio-4-tetra-acetyl-D-glucosylaminopyrimidine Hydrochloride (XII; R = $CO{\cdot}CH_2Cl$).—Chloroacetyl chloride (1·7 g.) was added to a solution of the above compound (5 g.) in dry chloroform (200 c.c.). After 8 hours, most of the chloroform was removed *in vacuo* and ether (5 vols.) was added. The precipitated solid (6 g.) was collected and recrystallised from ethyl acetate from which the chloroacetyl derivative *hydrochloride* separated as a white microcrystalline powder, m. p. 163—164° (decomp.) (Found, in material dried at 100° : C, 41·6; H, 4·7; N, 11·4. $C_{21}H_{33}O_{10}N_5SCl,HCl$ requires C, 41·0; H, 4·8; N, 11·4%). Dissolution in water followed by rapid neutralisation with sodium hydrogen carbonate solution yielded the free base as fine white needles, m. p. 138—139°.

4-Amino-8-D-glucosylamino-5 : 6 : 7 : 8-tetrahydro-6 : 7-diketo-2-methylthiopteridine (XIII).—Freshly prepared 5 : 6-diamino-2-methylthio-4-tetra-acetyl-D-glucosidaminopyrimidine (0·5 g.) was dissolved in boiling ethanol (25 c.c.); ethyl oxalate (1 g.) and sodium methoxide (0·56 g.) were added. There was an immediate reaction and a yellow granular solid was deposited. After 1½ hours on the water-bath, this solid was collected, washed with ethanol, and dried. It was dissolved in cold water, and the pH of the solution adjusted to 6 with acetic acid. On cooling, yellow needles (0·25 g.) were deposited. Recrystallisation from water gave the *product* as pale yellow needles, m. p. 230—240° (decomp.) (Found, in material dried for 2 days at 140°/10^{-4} mm. : C, 39·0; H, 5·1; N, 16·9. $C_{13}H_{17}O_7N_5S,H_2O$ requires C, 38·5; H, 4·7; N, 17·3%).

The product gave a strongly positive Molisch reaction and in alkaline solution it exhibited an intensely blue fluorescence in ultra-violet light.

4-Amino-5 : 6 : 7 : 8-tetrahydro-6 : 7-diketo-2-methylthiopteridine (XV).—A solution of ethyl oxalate (0·73 g.) in ethanol (15 c.c.) containing sodium ethoxide (from 0·46 g. of sodium) was heated to boiling and then added to a saturated solution of 4 : 5 : 6-triamino-2-methylthiopyrimidine (1·9 g.) in alcohol (35 c.c.), causing immediate deposition of a yellow solid. After 16 hours at room temperature this solid (2 g.) was collected and purified by dissolution in aqueous ammonia, treatment with charcoal, and reprecipitation with dilute hydrochloric acid. The *product* finally separated from dimethylformamide in pale yellow needles (Found, in material dried at 120° : C, 37·5; H, 3·3; N, 30·8. $C_7H_7O_2N_5S$ requires C, 37·3; H, 3·1; N, 31·1%). Alkaline solutions exhibited an intense blue fluorescence in ultra-violet light.

Grateful acknowledgment is made to the Department of Scientific and Industrial Research for a Senior Award (to H. S. F.), to Imperial Chemical Industries Limited, and to the Commonwealth Scientific and Industrial Research Organisation, Australia, for scholarships (to R. H. and H. J. R. respectively).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 15th*, 1950.]

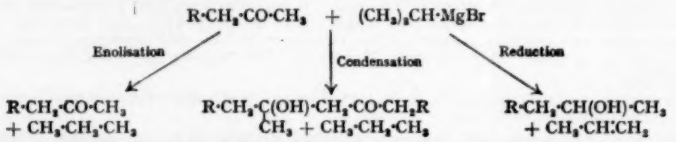
2. *The Anomalous Reactions of Grignard Reagents. Part II.*

By H. J. Shine.

Several methyl ketones, COMeR (R = Me, Et, Pr^{i}, Bu^{i}, Bu^{t}), have been treated with Pr^{i}MgX and Bu^{s}MgX (X = Cl, Br, I) under controlled conditions. The gaseous products of reaction have been measured, and the percentage of saturated and unsaturated hydrocarbon components determined. It has been found that the proportion of enolisation and condensation to reduction caused by these Grignard reagents follows the order RMgCl > RMgBr > RMgI; anomalous reaction is incomplete unless an excess of Grignard reagent is used. The rôle of an addition complex in anomalous reaction is discussed, and it is suggested that anomalous reaction involves the attack by other molecules on an addition complex, rather than various modes of rearrangement of a single complex.

Continuation of the investigation of anomalous reactions of Grignard reagents has shown the importance of the influence of the Grignard reagent halogen on anomalous reaction. Earlier studies by other workers on the effect of the halogen on anomalous reaction have shown conflicting results. Grignard and Savard (*Bull. Soc. chim. Belg.*, 1927, **36**, 97) found that, in the reaction of pulegone with alkylmagnesium halides, the extent of enolisation decreased with increasing atomic weight of the halogen atom. On the other hand, Grignard and Blanchon (*Bull. Soc. chim.*, 1931, **49**, 28), working with menthone and alkylmagnesium halides, concluded that, in general, the extent of enolisation is expressed by the order RMgCl < RMgBr > RMgI. Kharasch and Weinhouse (*J. Org. Chem.*, 1936, **1**, 220) reported that *n*-butylmagnesium bromide causes less reduction of benzophenone than does the chloride. Kharasch, Morrison, and Urry (*J. Amer. Chem. Soc.*, 1944, **66**, 368) found that methylmagnesium iodide causes the reduction of 2 : 4 : 6-trimethylbenzoyl chloride to the benzil, whereas the corresponding bromide does not. Shine and Turner (*J. Inst. Petroleum*, 1950, **36**, 73; Part I) have shown that pinacone undergoes condensation and reduction to 2 : 2 : 3 : 6 : 6-pentamethylheptane-3 : 5-diol in the presence of *iso*propyl- and *sec.*-butyl-magnesium bromides, but not in the presence of the corresponding chlorides.

In the present study a number of methyl ketones was treated with Grignard reagents that give saturated and unsaturated hydrocarbons as a consequence of anomalous reaction :



The effect of the halogen was determined by measuring the amount of gas evolved during reaction under controlled conditions, and determining the percentage constitution of the gas with respect to saturation and unsaturation. In Table I are given the results of these measurements. The volumes of the saturated gas are taken as a direct measure of the extent of enolisation and condensation, while those of the unsaturated gas are taken as that of reduction.

From Table I it can be seen that the total volume, representing total anomalous reaction, expresses the well-known effect of group size on extent of reaction; that is, COMeBu^{t} > COMePr^{i} > COMeEt > COMe$_2$. This relation holds for all the Grignard reagents, RMgCl, RMgBr, RMgI, used. The Grignard reagents differ markedly, however, in the ratio saturated gas : unsaturated gas. For each of the ketones this ratio follows the order RMgCl > RMgBr > RMgI. (In Table I this ratio is expressed as percentage of unsaturated gas in the gaseous product.)

Discussion.—The intention of this work was to obtain further knowledge of the way in which the nature and extent of the products formed in Grignard reactions depend on the halogen atom of the Grignard reagent, and to apply the results obtained to the currently accepted mechanisms of Grignard reactions. In discussing and so applying the results, it will be first assumed that these mechanisms are correct; later, however, it will be shown that the mechanisms are not entirely satisfactory, and modifications will be suggested.

The mechanisms by which are formed the several products of the reaction between a Grignard

reagent and a carbonyl compound are currently believed to involve the breakdown and rearrangement of a complex consisting of Grignard reagent and carbonyl compound. Certain refinements have been made in the pictorial representations of the addition-complex mechanisms since Hess and Rheinboldt (*Ber.*, 1921, **54**, 2043) and Grignard *et al.* (*Compt. rend.*, 1923, **177**, 299; *Ann. Chim.*, 1928, **9**, 5; *Bull. Soc. chim. Belg.*, 1927, **36**, 97) first suggested that the products corresponding to normal addition, reduction, enolisation, and condensation arose from rearrangements and breakdown of an intermediate complex, but the necessity for the existence of such a complex is still generally accepted. This necessity has been recently claimed from work on asymmetric reduction of carbonyl compounds with Grignard reagents (Vavon, Rivière, and Angelo, *Compt. rend.*, 1946, **222**, 959; Vavon and Angelo, *ibid.*, 1947, **224**, 1435; Mosher, Foley, and LaCombe, Abstracts of Papers, 115th Meeting of the American Chemical Society, page 1L; *J. Amer. Chem. Soc.*, 1950, **72**, 3994), and has been demonstrated kinetically for the reaction of Grignard reagents with nitriles (Swain, *J. Amer. Chem. Soc.*, 1947, **69**, 2306).

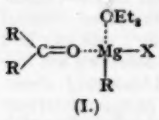
TABLE I.[a]

Volumes and percentage unsaturation of gaseous hydrocarbons evolved during Grignard reaction.

	$COMe_2$.			COMeEt.			$COMePr^i$.			$COMeBu^t$.			$COMeBu^i$.		
	b.	*c.*	*d.*	*b.*	*c.*	*d.*	*b.*	*c.*	*d.*	*b.*	*c.*	*d.*	*b.*	*c.*	*d.*
Pr^iMgCl	975	43·5	8·8	1440	64·2	12·2	1840	82·0	10·2	2130	95·0	13·8	1660	74·0	7·3
	—	—	—	1430	63·8	12·5	—	—	—	2060	92·0	13·3	1660	74·0	7·3
Pr^iMgBr	865	38·6	11·1	1250	55·8	16·5	1765	78·8	14·2	2130	95·0	18·7	1510	67·5	8·7
	885	39·2	12·1	1290	57·5	17·3	1855	83·0	15·0	—	—	—	1590	71·0	8·4
Pr^iMgI	725	32·4	26·7	1120	50·0	30·6	1735	77·5	26·1	2015	90·0	27·0	1425	63·5	13·7
	730	32·6	26·5	—	—	—	1675	74·7	25·7	1960	87·5	27·1	1410	63·0	13·7
Bu^sMgCl	1535	68·5	15·6	1610	71·8	17·8	1795	80·0	13·4	1900	84·8	20·0	—	—	—
	1480	66·0	15·8	1635	73·0	17·3	—	—	—	1900	84·8	20·0	—	—	—
Bu^sMgBr	1430	63·8	22·4	1730	77·2	27·1	1970	88·0	20·8	2060	92·0	28·1	—	—	—
	1360	60·6	22·3	—	—	—	1900	84·8	21·1	1860	83·0	27·7	—	—	—
Bu^sMgI	855	76·3	32·9	785	70·0	38·1	885	79·0	36·1	925	82·5	39·1	—	—	—
	715	63·8	31·0	800	71·5	37·8	830	78·0	34·5	835	74·0	40·0	—	—	—

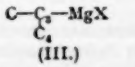
(*a*) This table represents reaction of 0·1 mole of ketone with 0·22 mole of Grignard reagent, except in the case of the Bu^sMgI reactions, in which 0·05 mole of ketone and 0·11 mole of Grignard reagent were used. (*b*) Total volume of gas obtained in ml. at N.T.P. (*c*) Percentage of theoretical yield of gas based on ketone. (*d*) Percentage of unsaturated gas in (*b*).

The use of addition complexes in reaction mechanisms connotes geometrical influences of the molecules involved. This connotation has been used in the cases of asymmetric reduction above, and also, earlier, in explaining the change in the types of products accompanying alterations in the constituent groups of the Grignard reagents and carbonyl compound, in the sense that these geometrical influences are exerted *within* the complex. In view of this it would be of interest to construct scale models of such complexes, the examination of which would show how great geometric influences really are. This is not possible, however, since some of the bond distances involved may be anything between those of covalent bonding and the unknown minima for co-ordination. Nevertheless, since the steric effects within a complex such as (I) will be greatest when the groups are as closely bonded as possible, one can obtain some idea of the magnitude of these effects by constructing models in which the atomic radius and bond angles of tetrahedral magnesium are used (Pauling, " The Nature of the Chemical Bond," 2nd edn., Cornell Univ. Press, Ithaca, N.Y., 1944, p. 179), and in which all bonds are single covalent.



(I.)

(II.)



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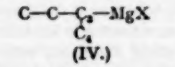
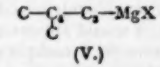


(IV.)



(V.)

In this way, for example, it is found that, in the four complexes (I) constructed from a methyl ketone (II) and the Grignard reagents (III), (IV), and (V), the alkyl groups R (denoted in skeletal form in III, IV, and V) can be brought into positions such that the least distance between the carbon atom C_1 and a hydrogen atom H_4 is the same for each complex, and similarly the least distance between a hydrogen atom H_3 and a carbon atom C_3 is the same for each complex. H_3 designates a hydrogen atom attached to the carbon atom C_3, and H_4 designates a hydrogen atom attached to a carbon atom C_4. The C_1–H_4 distance is that associated with bond formation

during reduction, while the H_3–C_3 distance is that associated with enolisation. In the rigid models described, these distances, measured between atomic centres, are respectively 2·04 A. and 1·76 A. The C–H distance in alkanes is approximately 1·09 A., so that if one may draw a conclusion from the measurements in the models, it is that one would expect enolisation to occur always in greater proportion than reduction. The Grignard reagents (III), (IV), and (V), are respectively *iso*propyl-, *sec.*-butyl-, and *iso*butyl-magnesium halide, and it has been shown (Shine and Turner, *loc. cit.*) that in reactions of these reagents with ketones the extent of enolisation is generally greater than that of reduction for *iso*propyl-, approximately equal to that of reduction for *sec.*-butyl-, and much less than that of reduction for *iso*butyl-magnesium halides. Results of a similar nature are well known in the literature. Thus the influence of the alkyl groups on the formation of reaction products must be largely other than steric: that is, apart from the fact that steric hindrance may prevent normal addition and thus enhance anomalous reaction. That the formation of reaction products depends more on the bond making and breaking contributions of the constituent groups than on their size is even more apparent from the halogen variation. Geometrically, as found in the models, the halogen in the complex is intramolecularly entirely without influence, and this situation is not to be altered by the fact that the bond lengths in the complex are likely to be different from those used in its model. The results summarized in Table I, however, show that there is an ordered change in both the nature and the extent of reaction products in going from chloride to iodide; the extent of total anomalous reaction decreases, and the extent of reduction increases. This change can be due only to electronic contributions of the halogen atom. Since these contributions are an inherent character of the Grignard reagent, it become necessary to decide whether the effects they cause in reaction are due to their operation before reaction occurs or after the formation of a complex. Thus it has been argued by Kharasch, Morrison, and Urry (*loc. cit.*) that, in the presence of cobaltous chloride, methylmagnesium bromide behaves like the corresponding iodide, since that tendency possessed by the iodide to operate as a free radical, when the occasion is suitable, is created in the bromide by the cobaltous chloride; and the argument is continued that alkylmagnesium iodides may react either as ions or as free radicals according to the suitability of the situation. In this way the electronic contributions of the halogen atom are in operation before the reaction takes place. Now, while it is an attractive hypothesis that reduction by Grignard reagents is due to free-radical reactions (see also Blicke and Powers, *J. Amer. Chem. Soc.*, 1929, **51**, 3380), and enolisation and condensation are due to ionic reactions (see Arnold and Liggett, *ibid.*, 1941, **63**, 3444; Evans and Pearson, *ibid.*, 1942, **64**, 2875), there is still doubt whether either of these particle processes can occur. The Mg–X bond is undoubtedly partly polar, but it is not so certain that alkyl carbanions exist and react as such in the ethereal solution. (It should be noted that the electrolyte property of ethereal Grignard reagent solutions is thought to be due to complex carbanions such as $[R_2MgX_2)^-$; the useful reactions of Grignard reagents, however, are also considered by Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., 1940, pp. 146, 329, 382, to be those of a carbanion.) And while Kharasch, Morrison, and Urry have given consideration to the reaction of free radicals with the ether solvent, one cannot overcome the fact that the solvent molecules should be sufficient inducement to free-radical formation should the formation of free radicals need induction. Yet, one can store ethereal solutions of Grignard reagents for long periods without serious loss in activity; one can boil under reflux ethereal solutions of alkylmagnesium iodides, provided that the solutions are free from excess of alkyl halide, also without serious loss in activity; Whitmore and George (*J. Amer. Chem. Soc.*, 1942, **64**, 1241) have shown the gaseous products of reaction to be quantitatively equivalent to anomalous reaction; the results of the present paper indicate a reproducibility that would be unlikely if solvent decomposition was not inconsiderable; and if solvent–free radical interaction was taking place, one would expect the amount of gaseous hydrocarbon to increase in going from chloride to iodide, whereas it decreases.

Hence, it would appear more reasonable that the electronic contributions of the halogen atom are operative in a complex during reaction, and not before reaction takes place. However, although this may be so, and although, similarly, the electronic contributions of the other groups in the reactants are to be manifested in a complex, there is, nevertheless, a number of observations that does not support the second part of the currently accepted addition-complex reaction sequence, namely, that the products of reaction result from the breakdown and rearrangement of the complex.

Numerous examples are known in which the action of water on unheated solutions of Grignard reagent plus carbonyl compound, or on the dry residues obtained by the evaporation of such solutions, gave back the unchanged carbonyl compound. Pfeiffer and Blank (*J. pr. Chem.*, 1939,

158, 243) clarified this part of Grignard chemistry with their work on benzophenone and some substituted benzophenones, in which they showed, first, that equimolar proportions of ketone and phenylmagnesium bromide give precipitates of complexes, which, when treated with water, regenerate the respective ketones; and secondly, that excesses of 100—300% of phenyl magnesium bromide are required to prepare the desired tertiary carbinols.

In the same way it can be seen from Table II that anomalous reaction is also incomplete if an excess of Grignard reagent is not used. Indeed, the sensitive colour test with Michler's ketone was not positive at the end of those reactions in which equimolar proportions of reagents were used, and in those in which a 10% excess of Grignard reagent was used, but it was positive when 100—120% excess of Grignard reagent was used.

TABLE II.

Effect of variation in concentration of iso*propylmagnesium bromide on extent of anomalous reaction.*

Ketone.	Gas, ml. at N.T.P.	Unsat. gas, %.	RMgX, mole.	Ketone.	Gas, ml. at N.T.P.	Unsat. gas, %.	RMgX, mole.	Ketone.	Gas, ml. at N.T.P.	Unsat. gas, %.	RMgX, mole.
COMeEt	840	18·9	0·10	COMeBu^i	1180	10·3	0·11	COMeBu^t	1620	17·1	0·10
	885	19·9	0·11		1175	10·7	0·11		1750	18·4	0·11
	885	19·3	0·11		1420	8·7	0·22		1860	18·2	0·11
	1160	16·5	0·22		1500	8·4	0·22		2040	18·7	0·22
	1200	17·3	0·22								

The indications are, therefore, that Grignard reactions, at least with carbonyl compounds, involve more than one molecule of Grignard reagent per molecule of second reactant. Further evidence that points in this direction is given perhaps by the formation of " coupling " products in many Grignard reactions. Particularly pertinent are the observations that in the reactions of *tert.*-butylmagnesium halide with allyl bromide, acetaldehyde, butyraldehyde, and *iso*-butyraldehyde (Whitmore, Stehman, and Hendron, *J. Amer. Chem. Soc.*, 1933, **55**, 3807), methyl ethyl ketone, and methyl *iso*butyl ketone (Shine and Turner, unpublished data), and various amides (private communication from Prof. E. E. Turner and Miss G. M. Owen, Bedford College, London), appreciable amounts of hexamethylethane are formed. It is well known that from reactions between *tert.*-butylmagnesium halide and *tert.*-butyl halide hardly any hexamethylethane is obtained, while attempts to prepare the latter by these reactions in the presence of cuprous chloride and cobaltous chloride were also without success (Shine and Turner, unpublished data). One would conclude, therefore, that the hexamethylethane is formed in the Grignard reactions, not by free-radical coupling, but by the attack of Grignard reagent on an addition complex of Grignard reagent and second reactant.

Thus, it appears from the evidence cited above that, although an addition complex is involved in Grignard reactions, the products of reaction are formed, not by various modes of rearrangement of this complex, but by the attack of other molecules on it. Where the geometric and electronic contributions of the constituent groups have their effect would then be in the manner in which a third molecule can approach and react with the complex. It is possible, in this collision mechanism, that the decrease observed in the extent of anomalous reaction in going from chloride to iodide may be due sterically to the increasing size of the halogen atom.

EXPERIMENTAL.

Reagents.—The halides and ketones used were fractionated through a column packed to a length of 4 ft. with Fenske helices, and fitted with a total-reflux, variable-take-off still head. A 1° range in b. p. was allowed in each case.

Preparation of the Grignard Solutions.—The following procedure was used for each halide except *sec.*-butyl iodide. 10 G. (0·41 g.-atom) of magnesium were covered with 50 ml. of dry ether in the usual three-necked flask set-up. To this was added 0·3 mole of the halide as a 10% solution in ether during 90 minutes, during which a further 150 ml. of ether were added in 50-ml. portions. When all the halide was added, the flask contents were boiled under reflux for 30 minutes, and the apparatus was flushed with nitrogen and then allowed to cool. The Grignard solution was then filtered by pumping it out of the flask, under nitrogen pressure, through a sintered-glass filter and into a graduated dropping-funnel. In later experiments the sintered-glass filter was replaced by a steel and glass filtration chamber, containing as the filter one of the conventional bacteria filter discs. The latter was found to be very rapid and efficient, and virtually unreactive toward the Grignard solutions. The graduated dropping-funnel was constructed so as to enable connection, by glass joints, to a gasometric analysis apparatus similar to that described by Gilman and his co-workers (*J. Amer. Chem. Soc.*, 1923, **45**, 155). The present apparatus was modified to enable the measurement of gas volume without making disconnections in the apparatus. After this apparatus had been used for determining the Grignard solution concentration, and parallel

acid back-titrations had been run for the same purpose, the latter method was found sufficiently accurate for its continued use in the present study, and hence the gasometric method was eventually discarded. A measured volume of the standardised Grignard solution was then drawn from the dropping-funnel into the nitrogen-flushed reaction flask.

With *sec.*-butyl iodide it was found that the Grignard reagent can be prepared in reasonable concentration only by using (*a*) slow addition of the halide solution to the magnesium, (*b*) vigorous stirring with a Hershberg stirrer, and (*c*) temperatures between −15° and 15°. At temperatures below −15° reaction of the halide with magnesium becomes very slow, and it tends to become uncontrollable if a large concentration of halide is allowed to build up and get warmer. Complementary to these requirements is that of not refluxing the solution until after filtration. Hence, in preparing *sec.*-butylmagnesium iodide, the solution was stirred at −15° for 2 hours after the addition of the halide solution, filtered, and refluxed for one hour, the apparatus flushed with nitrogen and allowed to cool, and then analysis was carried out. Good agreement was always obtained between the amount of halide used, the starting amount of magnesium, the magnesium undissolved, the amount of Grignard reagent formed, and the calculated amount of coupling that had taken place. The table below indicates this agreement, the halide used in coupling being calculated from the amount of magnesium consumed and the amount of Grignard reagent formed, all data being in g.-moles :

Halide used.	RMgX.	RX in coupling.	Accounted RX.
0·275	0·137	0·138	0·274
0·275	0·138	0·144	0·282
0·275	0·138	0·149	0·287
0·275	0·134	0·151	0·285

The reactions between *sec.*-butylmagnesium iodide and the ketones did not give the same consistency of results as was obtained with the other halides, however, and the total amount of anomalous reaction accompanying the former reactions seems inconsistently large. The *sec.*-butylmagnesium iodide solutions were always pale yellow, whereas the other Grignard solutions were colourless.

Reactions and Gas Measurements.—In each reaction, except those involving *sec.*-butylmagnesium iodide, 0·1 mole of ketone was added as a 10% solution in dry ether to 0·22 mole of Grignard solution at room temperature. The times of addition (in minutes) were 35 for $COMe_2$, 45 for COMeEt, 60 for $COMePr^i$, and 75 for $COMeBu^s$ and $COMeBu^i$. In the reactions with *sec.*-butylmagnesium iodide, 0·05 mole of ketone and 0·11 mole of Grignard reagent were used, the times of addition being half those of the above times. After addition of the ketone solution the mixture was boiled under reflux for one hour in the case of the *iso*propylmagnesium halides, and 2½ hours in the case of the *sec.*-butylmagnesium halides.

The method of analysing the gaseous products from the *sec.*-butyl Grignard reactions differed from that of the *iso*propyl Grignard reactions. In the latter case the gases were freed from ether by first passing through a water condenser, and then by passing up an 18″ jacketed tower packed with glass beads, and kept at −5° by alcohol–carbon dioxide. The gas was then collected in traps of known volume immersed in alcohol–carbon dioxide at −76°. At the end of the reaction time the traps were connected to a calibrated aspirator in a brine tank. The gas was allowed to boil into the brine-filled aspirator, the residual gas in the traps being expelled by filling them with water. After measurement of the volume of the gas in the aspirator at room temperature and pressure, samples were analyzed for olefin in an Orsat apparatus containing 83·5% sulphuric acid. In this way, after allowance for the known volume of dead-space air in the gas, the percentage of saturated and unsaturated gas could be calculated. The consistency of the results, and the earlier work of Whitmore (*loc. cit.*), justifies the assumption that the gas components were paraffin and olefin corresponding to the Grignard reagent used.

In the case of the *sec.*-butyl Grignard reactions, the scrubber was used at room temperature, and the amount of ether vapour in the gas mixture was determined in an Orsat apparatus containing 5% sulphuric acid. The olefin was determined as above, 87·5% sulphuric acid being used. Most of the experiments were repeated at least twice.

At least two blanks were run for each Grignard reagent in the manner described above, but with the exclusion of ketone. It was found, as is to be expected if unreacted halide is absent from the solution, that the effect of refluxing the Grignard solution is virtually negligible.

The financial support which made this research possible was obtained in part from a Parke-Davis Research Fellowship, and in part from the Industrial Science Research Institute of Iowa State College. In connection with the latter the author expresses his appreciation to Dean Ralph M. Hixon. The author is much indebted to Dr. George S. Hammond and Mr. William J. Meikle for their many discussions and suggestions.

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3. *Polarographic Behaviour of Iodo-compounds. Part I.*

By (Mrs.) E. Gergely and T. Iredale.

Organic iodo-compounds are reducible at the dropping-mercury cathode, hydrogen replacing the iodine which appears as the iodide ion. The half-wave potentials are independent of pH in the case of most non-ionizable compounds, but reduction of such compounds as acids and amines is pH dependent. The reduction is found to be a two-electron process, the general equation being:

$$RI + 2e + H^+ = RH + I^-$$

We record in this paper some polarographic studies, also the cathodic reduction on a larger scale, of some iodo-compounds, mainly aromatic, including iodobenzene. When the greater part of our work was completed there appeared an abstract, and subsequently the original account, of similar work on halogeno-compounds and iodobenzene itself (von Stackelberg and Stracke, *Z. Elektrochem.*, 1949, **53**, 118). Some of the Germans' conclusions are substantially the same as ours, but the compounds we used were usually different and our objectives were not quite the same.

In 1935 Brdička (*J. Gen. Physiol.*, 1935, **19**, 843) followed the hydrolysis of iodoacetic acid by observing the decrease in the height of the polarographic wave of the acid, attributing it to the elimination of iodine according to the equation: $CH_2I{\cdot}CO_2H + H^+ + 2e = CH_3{\cdot}CO_2H + I^-$. Proske (*Angew. Chem.*, 1943, **56**, 24) studied the polarographic reduction of halogeno-ketones and similar compounds, but was only concerned with the influence of the halogen on the half-wave potentials of the reduction of the keto-group. Lingane, Gardner, Swain, and Fields (*J. Amer. Chem. Soc.*, 1943, **65**, 1348) reported the reduction of iodophenylacridine in neutral and alkaline media in a two-electron step. In 1946 the reductions of iodofuchson (Stromberg and Reims, *J. Gen. Chem. Russia*, 1946, **16**, 1731) and of di-iodotyrosine and thyroxine (Simpson and Traill, *Biochem. J.*, 1946, **40**, 116) were reported. The first attempt to understand the mechanism of the polarographic reduction of halogenated organic compounds was made by Pasternak and von Halban (*Helv. Chim. Acta*, 1946, **29**, 190) who found that the half-wave potentials of ω-bromoacetophenone did not move to more positive values as the buffer medium was changed from alkali to acid, and they were led to assume that the mechanism was a direct electron addition and not a hydrogenation. But in the same year Keller, Hochweber, and von Halban (*Helv. Chim. Acta*, 1946, 29, 760), in a paper on the reduction of a series of chlorinated compounds, concluded that only the halogens bound to the aliphatic part of the compound were reducible at the dropping cathode. As this was not in agreement with the work of other investigators, we considered a study of the polarographic behaviour of iodo-compounds, especially wherein the iodine is bound to an aromatic carbon, would be of interest and importance.

All the compounds we examined proved to be reducible at the dropping-mercury cathode. The wave-heights for the compounds showed that two electrons were involved in the reduction, calculations being made by means of the Ilkovic equation: $n = i_d/605D^{\frac{1}{2}}cm^{\frac{1}{3}}t^{\frac{1}{6}}$, where n is the number of electrons involved, i_d the diffusion current in microampères, D the diffusion coefficient in cm.^{2} sec.$^{-1}$, c the concentration of the reducible substance in millimoles per litre, m the quantity of mercury dropping per second in mg., and t the drop-time in seconds. The diffusion coefficients were calculated indirectly from the diffusion coefficient of one of the substances, *i.e.*, *o*-iodobenzoic acid, by means of the Northrop–Anson formula: $D_1/D_2 = \sqrt{M_2/M_1}$, M_1 and M_2 being the molecular weights of the substance and the acid, respectively (Northrop and Anson, *J. Gen. Physiol.*, 1929, **12**, 543). The diffusion coefficient of the acid itself was obtained from its equivalent conductivity by means of the Nernst equation: $D = 2{\cdot}67 \times 10^{-7}\,\lambda_0/2\text{cm.}^2$ sec.$^{-1}$ (Askenary and Meyer, *Ber.*, 1893, **26**, 1354), and has the value $0{\cdot}854 \times 10^{-5}$ cm.^{2} sec.$^{-1}$. We also found that two electrons were involved in the reductions when large-scale operations were carried out in an apparatus similar to that described by Lingane and co-workers (*loc. cit.*). The amount of electricity required for the reduction of a sample was always in agreement with the theoretical value calculated for a two-electron process, *e.g.*, for the reduction of one gram of *o*-iodobenzoic acid to benzoic acid 784 coulombs were needed, whilst the theoretical value would be 780 coulombs where two electrons were involved. The reduction products were identified and we found in each case that the iodine had been replaced by hydrogen, and the iodine split off in the form of the iodide ion. The latter was estimated, and about 70% of the expected amount was usually found in the cathode vessel. Some iodide was also found in the anode vessel, and this must be due to inter-diffusion. No hydrolysis of the iodo-group occurred

under our experimental conditions, except in the case of iodoacetic acid. The heights of the polarographic waves of the aromatic iodides did not decrease after storage even in the alkaline buffers and other supporting electrolytes, and the reduction products never showed traces of phenolic hydroxyl groups when tested with ferric chloride. Our investigations seem to show that the polarographic waves of these compounds are due to the total reaction: $RI + 2e + H^+ = RH + I^-$, suggested by Brdička (*loc. cit.*) for iodoacetic acid.

The wave-heights were proportional to the concentrations of the solutions, but the slopes of the waves were found to be less steep than would be expected for two-electron reductions. The usual logarithmic plots ($\log \frac{i}{i_d - i}$ against potential, E,) were found to be of the order of 0·09 v. per log. unit unstead of the theoretical value, 0·03 v. Both the half-wave potentials and the wave-slopes proved to be very sensitive to experimental conditions, *e.g.*, to the ionic strength, the alcoholic content of the solution, and the nature of the cations of the supporting electrolyte. In some cases a slight shift of the half-wave potential to more negative values was observed when the concentration of the solution was increased. However, by keeping all experimental conditions rigorously constant from one run to another, we could reproduce both wave-height and half-wave potential very well. We have mentioned that Pasternak and von Halban (*loc. cit.*) noticed that the half-wave potential of certain halogenated compounds was independent of the pH of the supporting electrolyte, a fact also discerned by von Stackelberg and Strake (*loc. cit.*). Our experiments seemed to show that although this might be true for one series of iodo-compounds such as the iodo-derivatives of hydrocarbons, it was not the case for such substances as the iodobenzoic acids and the iodoanilines. It has been shown by Laitinen and Wawzonek (*J. Amer. Chem. Soc.*, 1942, **64**, 1765, 2365; 1946, **68**, 2541) that the half-wave potentials of the unsaturated hydrocarbons do not shift with the pH of the solution. The authors suggest that the reduction of the double bond takes place according to the general reaction, $[R] + 2e + 2H^+ = [RH_2]$, which is made up of the several part reactions: (1) $[R] + e = [R]^-$, (2) $[R]^- + e = [R]^{--}$, and (3) $[R]^{--} + 2H_2O = [RH_2] + 2OH^-$, (where $[R] = R'CH{:}CHR''$). The first step, *i.e.*, addition of the electron, is the potential-determining step. However, the half-wave potentials of maleic and fumaric acids *do* shift with the pH (Vopicka, *Coll. Czech. Chem. Comm.*, 1936, **8**, 349) showing that hydrogen ions play an important part in the reduction of these compounds, although the reducible group is again the double bond as in the previously mentioned compounds. The situation is complicated because the pH of the solution has also a great effect on the proportion of ions and molecules present. It is possible that double bonds may be reduced by two different mechanisms.

We have noticed a similar behaviour in the case of the iodo-compounds. The general equation, $RI + 2e + H^+ = RH + I^-$, may be compounded in the case of pH-independent reductions, of the following steps: (1) $RI + e = RI^-$, (2) $RI^- = R + I^-$, (3) $R + e = R^-$, (4) $R^- + H_2O = RH + OH^-$, the addition of the electron being the potential-determining step. We have listed in the table the half-wave potentials at 25° of a number of iodo-compounds in M/100-tetraethylammonium bromide as supporting electrolyte. The solutions contained 66% by volume of ethanol and 1/3 millimol./litre of the reducible compound. Potentials are referred to the saturated calomel electrode (S.C.E.) as zero.

The differences in the potentials for different compounds and isomers are very interesting, and something may be deduced from them without departing greatly from current theories. Maccoll (*Nature*, 1949, **163**, 178) has shown that with some hydrocarbons polarographic reductions proceed at potentials determined by the energy of the first unoccupied molecular orbital. If we assume that the addition of the electron in the case of iodo-compounds occurs at the first unoccupied orbital of the bond which is subsequently broken, it should occur with greater ease the lower the electron density at that bond (Wheland and Pauling, *J. Amer. Chem. Soc.*, 1935, **57**, 2086). It is easy to understand why the electron adds on more easily to *m*-iodotoluene (1·613 v.; not greatly different from iodobenzene, 1·616 v.) than to the *o*- and *p*-derivatives (1·656 v. and 1·660 v.). Substitution of the methyl group in the benzene ring produces by hyperconjugation a greater electron density in the *o*- and *p*-positions than in the *m*-. The electrophilic reagent, iodine, goes more readily to the *o*- or *p*-positions. ***But the reverse of this, removal of the iodine by polarographic reduction, goes more readily from the*** m-*position*.

The greater ease with which α-iodonaphthalene is reduced (1·506 v.) compared with β-iodonaphthalene (1·560 v.) is not quite so easy to explain, but it may be compared to the reactivity of sodium with naphthalene, where the sodium adds on more readily in the α-position. Here the electron comes from the sodium atom.

The half-wave potential for *p*-iodonitrobenzene (1·71 v.) seems anomalous, because the

nitro-group should decrease the electron density least at the *m*-position, and the potential for the *p*-derivative should be comparable with or lower than that of iodobenzene. We found, however, that *p*-iodonitrobenzene had two half-wave potentials: the first one is due to the reduction of the nitro-group, and the second to the iodine. We are dealing, then, at this second potential with the reduction, not of the nitro-compound, but of *p*-iodoaniline, which itself has a half-wave potential of this order (1·716 v.), and this is quite understandable, as the amino-group by its resonance properties enhances the electron density at the *p*-position. However, both these iodo-compounds show a pH dependence which we have yet to investigate further.

Half-wave potentials (in volts) in M/100-*tetraethylammonium bromide*; 66% *ethanol*; *concentrations* 1/3 *millimol./litre*; *temp.* 25°. *Potentials are referred to the saturated calomel electrode.*

Iodobenzene	−1·616	α-Iodonaphthalene	−1·506	2-Iodo-1 : 4-dimethoxy-benzene	−1·446
m-Iodotoluene	−1·613	β-Iodonaphthalene	−1·560	*p*-Iodonitrobenzene	−1·710
o-Iodotoluene	−1·656	4-Iodoacenaphthene	−1·620	*p*-Iodoaniline	−1·716
p-Iodotoluene	−1·660				

The iodobenzoic acids, iodoacetic acid, and *o*- and *p*-iodoaniline were also investigated, and were found to have half-wave potentials dependent on the pH of the solution. *o*-Iodobenzoic acid gives two steps (1·04 v. and 1·60 v.) in N/10-potassium chloride, and also two steps (1·14 v. and 1·60 v.) in tetraethylammonium bromide and 66% alcohol, the sum of the two wave-heights being, in each case, proportional to the concentration of the acid. In buffered solutions the two steps are not obtainable in one polarogram, as the hydrogen decomposition in acid buffers precedes the second step, whilst in the alkaline buffers only the second step is present. In buffers from pH 1·12 to pH 12·5 the measurable half-wave potentials were shifting from 1·00 v. to 1·64 v.

m-Iodobenzoic acid gives only a very wide wave in potassium chloride solution and in tetraethylammonium bromide. The separation of the two waves was not possible. The reduction of the *m*-acid in acid buffers starts at somewhat lower potentials than the hydrogen discharge, but it is very close to it from the point of view of the measurement, which is rendered very difficult. In alkaline buffers the half-wave potential is 1·605 v.

p-Iodobenzoic acid never reduces at potentials lower than those of the hydrogen discharge. Only in alkaline buffers is a definitive half-wave (1·58 v.) obtained.

The half-wave potentials of iodoacetic acid shift from 0·17 v. to 0·67 v. when the pH is increased from 1·12 to 12·5.

The iodoanilines show maxima in acid buffers, but in alkaline buffers and in tetraethylammonium bromide no maxima were obtained.

These pH-dependent iodo-compounds, on account of their ionization and difference in properties of the molecule and the ion, are being investigated in greater detail.

Experimental.

The polarographic apparatus was of the manually controlled, conventional design. The dropping cell was connected by an agar–saturated potassium chloride bridge to a saturated calomel electrode, prepared from pure mercury, calomel, and potassium chloride (supplied by Leeds and Northarop). The cell and electrode were contained in a thermostat at 25° ± 0·1°. Purified hydrogen was bubbled through the solutions to remove dissolved oxygen. The characteristics of the capillary were: m = 0·9166 mg., t = 5·44 seconds. The 50-ohm coil resistance galvanometer was shunted and calibrated with a standard microammeter in series.

Buffers: pH 1·2 to 5·3, were made from N/5 hydrochloric acid and N/5-sodium acetate; pH 5·3 to 8·20, from N/5-potassium dihydrogen phosphate and N/5-disodium hydrogen phosphate; pH 8·2 to 12·6, from N/5-sodium hydroxide, N/5-sodium chloride, and N/5-glycine.

The iodo-compounds used had all been carefully purified by recrystallization and vacuum sublimation by the group of workers engaged on spectroscopic studies of these compounds.

We are indebted to Dr. B. Breyer for helpful discussion. We gratefully acknowledge financial assistance from the Commonwealth Science Grant to this University.

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4. *Further Studies on the Stereochemistry of Aromatic Ethers.*

By K. B. Everard and L. E. Sutton.

The electric dipole moments of five arylene dimethyl diethers (IV)—(VIII) have been measured, and compared with those previously found for others of the series [(I)—(III)] (*J.*, 1949, 2312). Views put forward in the latter paper are thereby supported. There is a tendency for all the methoxy-groups to lie coplanar with the aromatic rings, but this is overridden in (VI), (VII), and (VIII) by steric interference, so that the substituents in these three compounds lie in planes almost orthogonal to those of the rings. The moment of hexamethoxybenzene has also been measured, but the stereochemistry is too complicated for the value (2·05) to be unambiguously interpreted.

Recently (*J.*, 1949, 2312) we reported that the electric dipole moments of 1 : 5- and 1 : 4-dimethoxynaphthalene (I, 0·67 D.; II, 2·09 D.) were not the same as that of quinol dimethyl ether (III, 1·73 D.). The moment of the last compound is usually ascribed to the free rotation of the angular methoxy-groups about the C_{aryl}–O bonds; the same result would, however, follow if these groups were constrained to lie in the plane of the ring, but were free to assume the *cis*- or the *trans*-configuration in equal degree. It was suggested that in all three compounds the increase in the C_{aryl}–O bond order brought about by resonance imposes this constraint. In the case of the naphthalene derivatives the configurations with the methoxy-groups lying *cis* to the *peri*-hydrogen atoms are believed to be extremely improbable, because of the steric interference between these atoms and the methyl groups.

If this hypothesis is correct, we should predict that 1 : 5-dimethoxyanthracene (V) would have a small moment like that of (I). 9 : 10-Dimethoxyanthracene (VI), however, because it has *peri*-hydrogen atoms on both sides of each methoxy-group, could not assume a planar configuration at all, and would have to exist with the planes of its methoxy-groups roughly orthogonal to the anthracene ring plane; these could take up *cis*- and *trans*-configurations (with respect to each other) equally, so the compound should have much the same moment as quinol dimethyl ether (III). Further confirmation would come from the moments of 9 : 10-dimethoxy-1 : 2-benz- and 9 : 10-dimethoxy-1 : 2-5 : 6-dibenz-anthracene (VII and VIII), which from the preceding argument should also be close to that of (III).

We must next consider how coplanar the " coplanar " configurations are. As has previously been remarked (Everard and Sutton, *loc. cit.*), the actual moments of (I) and (II) are respectively not as small or as large as would be required if the compounds were perfectly flat ($\mu_I = 0$; $\mu_{II} = 2{\cdot}45$); so we may consider the possibilities: (*a*) that the equilibrium positions of the methoxy-groups are coplanar, but the weakness of the π-bonding permits considerable oscillation; (*b*) that owing to the steric interference between the methyl groups and the β-hydrogen atoms, there are equilibrium positions on each side of the ring plane (see Fig. 1 of previous paper; in the caption thereto the words *cis* and *trans* should be interchanged); or (*c*) that the π-bonding is strong enough to compel the groups to be coplanar with the ring, but the *cis*- are less probable than the *trans*-configurations because the repulsion between the methyl groups and the *peri*-hydrogen atoms is greater than that between the methyl groups and the β-hydrogen atoms.

Some elimination of these alternatives should be possible from the new measurements: thus if (*c*) were correct, we should expect the moment of (VIII) to be markedly less than that of (VI) or of (VII) because, even if the *peri*-hydrogen atoms were not able to block the planar positions, the additional benzene rings certainly would.

By the kindness of Professor J. W. Cook, F.R.S., who lent us specimens of (V), (VII), and (VIII), we have been able to complete measurements on this series.

The importance of the major hypothesis in application to benzene derivatives has been further investigated by measuring the moment of 2 : 5-dibromoquinol dimethyl ether. Hexamethoxybenzene was examined in an attempt to discover how the methoxy-groups in it are disposed.

Discussion.

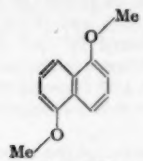
From the results for (V)—(VIII) collected in Table IV and repeated beneath the formulæ, it is clear that all the essential predictions from our major hypothesis are verified. We therefore conclude that there is π-bonding between the methoxy-groups and the aromatic rings strong enough to produce approximate fixation in the plane of the rings, unless a *peri*-hydrogen atom gets in the way. In this case, the methoxy-group is either restricted to one planar orientation

or, if there are two *peri*-hydrogen atoms, it projects roughly orthogonally from the plane of the ring.

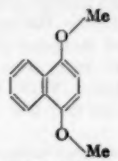
Jones has examined the ultra-violet absorption spectra of 10-methoxy- and of 9-methoxy-10-methyl-1 : 2-benzanthracene, and has also concluded that the methoxy-groups project orthogonally (*J. Amer. Chem. Soc.*, 1945, **67**, 2127). In addition, Badger and Lynn (*J.*, 1950, 1726) have just postulated this to explain the anomalous rate of addition of osmium tetroxide to (VII).

The fact that (IV) has a moment so much less than that of (III) indicates either a marked restriction of rotation of the methoxy-groups by the bromine atoms, or a combination of π-bonding and obstruction of a planar position.

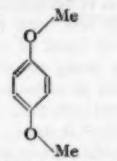
It is now necessary to consider how much more detailed information about the stereochemistry of these compounds can be extracted from the results.



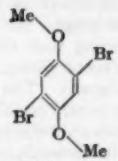
(I.) 0·67



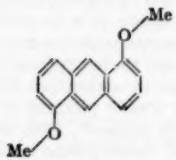
(II.) 2·09



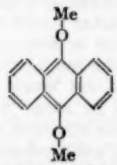
(III.) 1·73



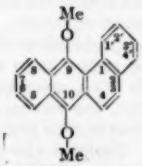
(IV.) 1·01



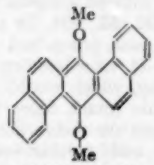
(V.) 0·63



(VI.) 1·73



(VII.) 1·65



(VIII.) 1·67

Numerals refer to dipole moments (D.)

First, the mathematical treatment of the moment of a compound with two rotating polar groups must be extended. This is done in an appendix following this section.

If now we suppose that there is free rotation within limits (*i.e.*, half-amplitude = $\theta = \theta' = \theta''$; see appendix) of the two methoxy-groups in 1 : 5-dimethoxynaphthalene, 1 : 5-dimethoxyanthracene, and 2 : 5-dibromoquinol dimethyl ether, estimate θ from scale models,* and then calculate the moments expected for these molecules by equation (6) in the appendix [taking μ as 1·22, from the moment of (III) and equation (8)], we find for each compound that $\theta \approx 110°$ (relative to *trans* planar positions) and $\mu_{total} \approx 1{\cdot}5$. This value of μ_{total} is much too high. The corresponding value, 1·9, for 1 : 4-dimethoxynaphthalene is too low. Such calculations confirm our hypothesis that these moments are due to somewhat imperfect planar fixation by π-bonding (cf. previous paper; the interpenetration of the van der Waals zones is *ca.* 0·1 A. between the methyl group and an *o*- or β-hydrogen atom, but *ca.* 0·9 A. with an *o*-bromine atom and *ca.* 1·1 A. with a *peri*-hydrogen atom).

The half-amplitudes of free oscillation, $\pm\theta$, necessary to give the observed moments are 63° for 2 : 5-dichloro- and 2 : 5-dibromo-quinol dimethyl ether, 40° for 1 : 5-dimethoxynaphthalene †, 37° for 1 : 5-dimethoxyanthracene, and 83° for 1 : 4-dimethoxynaphthalene †. A possible explanation of these differences, *viz.*, that π-bonding is loosened when there are two methoxy-groups on the same benzene ring, was put forward in the previous paper.

Scale models show that, whatever the orientation of the 9-methoxy-group in (VII) and (VIII), it touches the 8- and 1′-hydrogen atom. There is least overlap, *ca.* 0·2 A., of the methyl group with each such hydrogen atom when the plane containing the methoxy-group is inclined

* Wooster models have been used (Wooster, McGowan, and Moore, *J. Sci. Instr.*, 1949, **26**, 140). These have conventional van der Waals radii. It has been assumed that the C–$\widehat{O}$–Me angle is 120°, and that methyl groups in contact with unbonded atoms are rotated about the C–Me bonds so as always to present the minimum van der Waals "radius" towards the interfering atom. If the van der Waals zone of a methyl group were taken as the volume it sweeps out when it rotates, the interpenetration in a coplanar anisole molecule would be ~1 A.

† The values given in the previous paper are erroneous.

towards the 8-hydrogen atom at an angle of about 80° to the plane of the rings. This disposition would make the moment of (VIII) somewhat less than that of (VI) [equation (6): for *trans*-molecule $\psi' - \psi'' = \pi$; for *cis*, $\psi' - \psi'' > 0$], while that of (VII) would remain the same as that of (VI) [see equation (8)]. The value calculated for (VIII), on this basis, is 1·71.

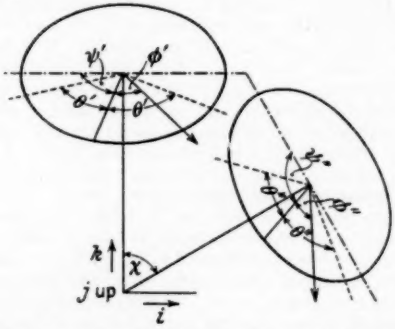
A further complication is the possibility that the oxygen atoms of the methoxy-groups in (VIII) would be forced out of the plane of the anthracene ring (cf. the case of 4 : 8-dichloro-1 : 5-dimethoxynaphthalene discussed in the previous paper). It is only possible to estimate the extent of this deflection very crudely; but if it is sufficient to relieve half the van der Waals overlap between the oxygen atoms and the " benz " groups, then the C_{aryl}–O bonds are deflected through about 10°, and the methoxy-groups can then oscillate freely with a half-amplitude of about 20° about the equilibrium positions described above. These angles are approximately doubled if the deflection is sufficient to avoid any overlap at all. It is important to note that if a methoxyl-oxygen atom is deflected upwards, its methyl group must also be above the plane of the rings. An attempt has been made to estimate the moments of (VII) and (VIII), by supposing that the C_{aryl}–O bond of each trapped methoxy-group is deflected 10° out of the anthracene plane, and by using equation (5) with what seem the best values for the several parameters. The moments so obtained for (VII) and (VIII) are 1·65 and 1·53 respectively.

It is only possible to conclude that such deflection may take place, but that these compounds provide no definite proof that it does.

The molecule of hexamethoxybenzene is too complex for rigorous treatment, but the moments to be expected for some possible dispositions of the methoxy-groups can be calculated. If each group rotated independently and freely, the moment would be $\sqrt{6}\mu = 3{\cdot}0$ (see Zahn, *Physikal. Z.*, 1932, **33**, 400, for the relevant equation). This value would also apply to a molecule in which each group had an equal probability of being up or down, in planes orthogonal to the ring. If the π-bonding were so strong as to require the methoxy-groups to lie coplanar with the ring, which would result in 0·5-A. overlaps of van der Waals zones in a swastika-shaped molecule (much more in others), the moment would be zero. Such simple pictures of the molecule are shown not to correspond to reality by the observed dipole moment, 2·05, which agrees with neither estimate. Perhaps the unmethylated compound, hexahydroxybenzene, would have a considerably smaller moment, owing to the substitution of repulsive forces by the attractive ones of hydrogen-bonding in the coplanar configuration. The dipole moment of this substance has not been measured.

Appendix.

In order to facilitate discussion of the experimental results, a general equation has been derived expressing the root mean square moment of non-rigid molecules such as quinol dimethyl ether and its derivatives.



Consider two vectors of scalar magnitude μ formally able to rotate about axes which are inclined at an angle χ, and to which the vectors are severally orthogonal. Angles relating to these two vectors will be distinguished by one or by two primes. For convenience let us define reference positions measured by the angles ψ' and ψ'' between them and the plane containing the two axes of rotation; and let the limits of rotation about these positions be through angles $\pm\theta'$ and $\pm\theta''$. The instantaneous positions of the vectors relative to the above reference positions are designated ϕ' and ϕ'' ($|\phi| \leqslant |\theta|$). We take as our system of rectangular Cartesian co-ordinates

the directions represented by i, j, and k, i and k being in the plane containing the axes of rotation, and k parallel to the one with a single prime. The components of any additional, fixed moments which the molecule may have are represented by μ_i°, μ_j°, and μ_k°, and their vector sum is μ°.

Thus the total moment of the molecule, μ_t, is given by the four equations:

$$\mu_i = \mu_i^\circ + \mu\,[\cos(\psi' + \phi') + \cos(\psi'' + \phi'')\cos\chi] \quad . \quad . \quad . \quad . \quad (1)$$

$$\mu_j = \mu_j^\circ + \mu\,[\sin(\psi' + \phi') + \sin(\psi'' + \phi'')] \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$\mu_k = \mu_k^\circ + \mu\cos(\psi'' + \phi'')\sin\chi \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$\mu_t^2 = \mu_i^2 + \mu_j^2 + \mu_k^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The next step is to integrate μ_t^2 over the ranges $\phi' = \pm\theta'$, $\phi'' = \pm\theta''$, in order to find the mean value $\overline{\mu_t^2}$. The following result is obtained (the abbreviations s′ and s″ are used for $\sin\theta'/\theta'$ and $\sin\theta''/\theta''$ respectively):

$$\overline{\mu_t^2} = \left(\int_{-\theta'}^{+\theta'}\int_{-\theta''}^{+\theta''} \mu_t^2 d\phi'\,d\phi''\right) \Big/ \left(\int_{-\theta'}^{+\theta'}\int_{-\theta''}^{+\theta''} d\phi'\,d\phi''\right)$$

$$= \mu^{\circ 2} + 2\mu\mu_i^\circ(s'\cos\phi' + s''\cos\psi''\cos\chi) + 2\mu\mu_j^\circ(s'\sin\phi' + s''\sin\psi'') + 2\mu\mu_k^\circ s''\cos\psi''\sin\chi + 2\mu^2 + 2\mu^2 s's''(\cos\psi'\cos\psi''\cos\chi + \sin\psi'\sin\psi'') \quad . \quad (5)$$

Certain special cases are useful: (1*a*) If $\mu^\circ = 0$, $\chi = 0$, and $\theta' = \theta''$,

$$\overline{\mu_t^2} = 2\mu^2\,[1 + s^2\cos(\psi' - \psi'')] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

(1*b*) If $\theta = \pi$, then

$$\overline{\mu_t^2} = \mu^{\circ 2} + 2\mu^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

(2) If there are equal numbers of each of two kinds of molecule, one kind with $\psi' = \psi_1'$ and $\psi'' = \psi_1''$, the other kind with $\psi' = \psi_2'$ and $\psi'' = \psi_2''$; and if $\mu^\circ = 0$ for each; and if $\psi_1' = \psi_2'$ and $\psi_1'' - \psi_2'' = \pi$ (corresponding to a mixture of *cis*- and *trans*-types), then:

$$\overline{\mu_t^2} = 2\mu^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

This result does not depend on all values of ϕ between $\pm\theta$ being equally probable; it holds for any distribution function which is the same for both ϕ' and ϕ'', as may be seen by multiplying each integrand for this particular case by a distribution function $f(\phi)$. The latter vanishes in the final expression for $\overline{\mu_t^2}$.

These results mean that a molecule such as quinol dimethyl ether would have the same moment whether (i) the methoxy-groups rotate freely [case (1*b*), with $\mu^\circ = 0$], (ii) they are fixed in equally probable *cis*- and *trans*-forms [case (2)], (iii) the groups in these *cis*- and *trans*-forms rotate freely within the limits $\pm\theta$ [case (2)], or (iv) the oscillation, not being free, is such that the probability of any angle of swing is some function of that angle, the same function applying to each group [case (2)].

Experimental.

Preparation and Purification of Materials.—AnalaR benzene was purified as before.

2 : 5-Dibromoquinol dimethyl ether was prepared by methylating the quinol. The latter, which had been made by Hammick, Hampson, and Jenkins (*J.*, 1938, 1263), was purified by two recrystallisations from water and by sublimation in a vacuum. The white crystals melted at 189·5—191°. 6 G. of these were heated under reflux with methyl sulphate (4 ml.) and sodium hydroxide (1·8 g.) in water (9 ml.) for 10 minutes. After trituration with 2N-sodium hydroxide to remove phenolic material, the solid product was twice recrystallised from ethanol and sublimed at 9 mm. The white crystals (1·1 g.) melted at 144—144·5° (Kohn and Guttmann, *Sitz. Akad. Wiss. Wien*, 1924, **133**, 573, give 142°).

Specimens of 1 : 5-dimethoxyanthracene and 9 : 10-dimethoxy-1 : 2-benz- and 9 : 10-dimethoxy-1 : 2-5 : 6-dibenz-anthracene were provided by Professor J. W. Cook, F.R.S., and had m. p.s of 231—232°, 136—139°, and 232—235° respectively (cf. Cook and Pauson, *J.*, 1949, 2726; 232—232·5°; Badger, Cook, and Ongley, *J.*, 1950, 873; 137—138°, 234—235·5°).

9 : 10-Dimethoxyanthracene was made by Meyer's method with minor modifications (*Annalen*, 1911, **379**, 70). After the methylation the product was triturated with 2N-sodium hydroxide, and recrystallised twice from ethanol and once from benzene, forming colourless plates with a strong blue fluorescence, m. p. 202° (cf. Meyer, 202°). After the last recrystallisation the substance was exposed only to dim red light until the dielectric constant measurements had been completed (it forms a photo-oxide).

A specimen of hexamethoxybenzene made in the Dyson Perrins Laboratory (see Robinson and Vasey, *J.*, 1941, 660; Baker, *ibid.*, p. 662) was recrystallised from water without change of m. p., 82°. The original material, which had been recrystallised from ligroin (b. p. 60—80°) was used.

Physical Measurements.—All measurements were carried out in benzene at 25°. Dielectric-constant measurements on 2 : 5-dibromoquinol dimethyl ether solutions were done with a condenser similar to the one described by Jenkins and Sutton (*J.*, 1935, 609); but since its volume is 50 ml. it cannot be used for scarce materials (only 0·05 g. of 9 : 10-dimethoxy-1 : 2-5 : 6-dibenzanthracene was available to us). Consequently, for the remaining compounds a modified Sayce–Briscoe type of condenser was used. It differs from that described by Le Fèvre ("Dipole Moments," Methuen, 1938, p. 32) in having, instead of leads to mercury cups, tubular brass connectors fitted with thumb-screws, and in having an earthed brass sleeve surrounding the lead to the inner plate. The advantage of the latter is that it obviates the need for keeping the water-surface in the thermostat either calm or at the same level. The condenser was silvered according to Sugden's recipe (*J.*, 1933, 770). Its volume is 6 ml. and its electrical capacity is 50 cm.

Solutions are made up in a small bottle with a standard neck and stopper. One limb of a 1-mm. bore ∩-shaped delivery tube is internally sealed to the top of the bottle and reaches right to the bottom; the other limb is internally sealed into a standard cone, which can be covered with a cap (this arrangement prevents wetting of the cone). The solute is weighed out from a microchemical balance into the dry, weighed bottle, and the dry solvent introduced through the ∩-tube from a reservoir by upward delivery given by pressure of dry air, under which the solvent is stored. The bottle is capped, stoppered, and weighed and, after dissolution has occurred, its contents are transferred to the condenser, which has a standard socket, by pressure of dry air. The same agency is later used to fill a 4-ml. Sprengel–Ostwald pyknometer directly from the condenser, and the remaining liquid is placed in one compartment of the refractometer cell. By this procedure the possibilitity of hygroscopic solvents being contaminated by atmospheric moisture is eliminated.

Refractive indices of all compounds were measured for Na_D light with a Pulfrich refractometer (Hilger, London), and those of the anthracene derivatives also at the other wave-lengths shown in Table I. Refraction values derived from these measurements are not very accurate for three reasons: first, the intensities of the 6438, 4800, and 4358 A. lines are rather low, especially with the use of a divided cell; secondly, the solutes absorbed some of the light; and thirdly, the Δn values were relatively small, because all the solutions used were dilute. The first difficulty was alleviated by placing a cylindrical lens (a tube of water) of the same focal length, f, as the cylindrical cell, in the path of the incident parallel beam at a distance of $2f$ from the cell. The light reaching the cell is hence divergent. On entering the cell it is, however, brought parallel again, and remains so when refracted downwards through the prism into the telescope; without the lens much of the light is lost.

Computation of Moments.—The notation used here is explained by Everard, Hill, and Sutton (*Trans. Faraday Soc.*, 1950, **46**, 417). The experimental procedure described above justifies the use of the method advocated in the latter paper for computing a, rather than the one suggested by Halverstadt and Kumler (*J. Amer. Chem. Soc.*, 1942, **64**, 2988). The dielectric constant of benzene at 25° was taken as 2·2727 (Hartshorn and Oliver, *Proc. Roy. Soc.*, 1929, *A*, **123**, 664; cf. values in a list given by Clay, Dekker, and Hemelrijk, *Physica*, 1943, **10**, 768). The specific volume of each batch of benzene was measured, and is recorded in Table IV under the heading v_1: v_1 and ε_1' are values obtained by the method of least squares from the v–ω and ε–ω graphs.

Molar refractions have been computed with the equation:

$$[R]/M_2 = [(n_1^2 - 1)/(n_1^2 + 2)] \cdot \beta + [6n_1v_1/(n_1^2 + 2)^2] \cdot \gamma + v_1(n_1^2 - 1)/(n_1^2 + 2)$$

(Everard, Hill, and Sutton, *loc. cit.*), in which the coefficients of β and γ, and the constant term, have the values c_1, c_2, and c_3 respectively in Table I. These are based on a specific volume of 1·14515 ml./g. for benzene at 25°, and on the observed n_λ^2 values shown in Table I.

TABLE I.

(These figures refer to benzene at 25°.)

Line.	Cd_r.	Na_D.	Hg_g.	Cd_g.	Cd_b.	Hg_v.
λ (A.)	6,438	5,983	5,461	5,086	4,800	4,358
$10^{-30}\nu^2$ (sec.$^{-2}$)	2,167	2,586	3,012	3,472	3,898	4,728
n_λ^2	2·23225	2·24398	2·25612	2·26971	2·28282	2·30962
$10^5\ c_1$	29,116	29,312	29,513	29,738	29,953	30,388
$10^5\ c_2$	57,312	57,145	56,973	56,781	56,596	56,222
$10^5\ c_3$	33,342	33,566	33,797	34,054	34,300	34,799

Molar dispersions, **D**, are expressed as $[R]_D - [R]_\infty$ (see Bauer and Fajans, *J. Amer. Chem. Soc.*, 1942, **64**, 3023). $[R]_\infty$ is estimated by the reciprocal plotting method of Wulff (*Z. physikal. Chem.*, 1933, *B*, **21**, 368), in which $1/[R]$ is plotted against the square of the frequency of the light (ν^2: Table I). This is a linear plot if there are no absorption bands near the frequency region examined. Even so, the extrapolation can be hazardous, owing to the visible region being but a small part of the spectrum, and to the uncertainties in the individual $[R]$ values noted in the last section. The probable uncertainty in **D** is indicated in the column headed $\pm$ in Table III.

It is common practice to take $[R]_D$ as a measure of the distortion polarisation of the solute molecules (*i.e.*, ${}_AP + {}_EP$). Therefore, since ${}_EP = [R]_\infty$, **D** represents the allowance made for ${}_AP$. With substances

having extensive conjugated systems (such as 9 : 10-dimethoxy-1 : 2-5 : 6-dibenzanthracene), dispersions ought to be measured, lest the ${}_{A}P$ allowance should be excessive (Everard, Hill, and Sutton, *loc. cit.*). All but one of the present anthracene derivatives have $[R]_D$ values agreeing within 1·5 c.c. with the values ($[R]_D$ (calc.) in Table IV) calculated from those of anthracene (65·4 c.c.; Steiger, *Ber.*, 1923, **56**, 998, and references therein), naphthalene (44·5), benzene (26·2), and anisole (33·0) (Landolt–Börnstein, "Tabellen"), so the ${}_{A}P$ allowance should not be more than usual in these cases; but as the value for 9 : 10-dimethoxy-1 : 2-5 : 6-dibenzanthracene shows an exaltation of 4·9 c.c. and the dispersion is large, the moment quoted for this compound may be too small by perhaps 0·05. However, in the absence of experimental ${}_{A}P$ data, no definite conclusions can be drawn, so all moments in Table IV are based on observed $[R]_D$ values therein. The latter are got from Δn–ω graphs, and they therefore differ slightly from those in Table III, which are obtained from single solutions. The column headed $\pm$ in Table IV gives the observational uncertainty in μ, and takes no account of uncertainties in ${}_{A}P$.

Results.—The experimental observations are given in Table II, where Roman numerals refer to the structural formulæ (p. 17), and to the names of the compounds printed against the same numerals below Table IV. The numerals in columns 1 and 2 of Table III, which gives the dispersion observations, correspond to those in Table II; values of Δn_D are omitted from Table III because they already appear in Table II.

TABLE II.

Compound.	Soln. no.	$10^6\omega$.	ε.	v.	$10^5\Delta n_D$.	Compound.	Soln. no.	$10^6\omega$.	ε.	v.	$10^5\Delta n_D$.
(IV)	1	2,858	2·2740	1·14321	—	(VII)	1	1,650	2·2755	1·14395	31
	2	4,701	2748	4206	—		2	9,265	2872	4140	168
	3	7,704	2762	4047	—		3	10,532	2893	4101	195
	4	9,169	2770	—	—						
	5	9,624	2774	3910	—	(VIII)	1	1,322	2745	4564	25
	6	69,830	—	—	319		2	5,015	2802	4437	106
							3	8,652	2860	4302	188
(V)	1	1,293	2736	4564	30						
	2	8,448	2782	4350	141	(IX)	1	1,818	2760	4410	—
	3	8,829	2784	4341	142		2	8,334	2872	4218	—
							3	10,995	2922	4140	4
(VI)	1	1,655	2757	4416	23						
	2	6,754	2850	4263	106						
	3	9,251	2896	4179	140						
	4	14,251	2984	4036	220						
	5	14,654	2993	4027	227						

TABLE III.

Compound.	Soln. no.	$10^5\Delta n_\lambda$.					$[R]_\lambda$.						D.	$\pm$.
		λ:	6438.	5461.	5086.	4800.	4358.	6438.	5893.	5461.	5086.	4800.	4358.		
(V)	3		142	153	160	182	—	80·4	80·9	82·8	84·2	88·0	—	9·2	2
(VI)	4		213	235	249	270	—	78·6	79·6	81·4	83·1	85·4	—	8·7	1
(VII)	3		193	206	223	235	272	98·7	99·2	101·3	104·3	106·6	113·1	11·9	2
(VIII)	3		183	200	214	—	—	118·9	120·5	123·6	127·0	—	—	15·1	2

TABLE IV.

Compound.	ε_1'.	$10^5\alpha$.	v_1.	v_1'.	$-10^5\beta$.	$10^5\gamma$.	${}_{T}P_2$.	$[R]_D$ (obs.).	$[R]_D$ (calc.).	μ.	$\pm$.
(IV)	2·2725	498	—	1·14491	594	46	76·2	55·5	55·4	1·01	0·05
(V)	2·2727	645	1·14609	1·14606	302	159	88·8	80·6	79·1	0·63	0·03
(VI)	2·2727	1820	1·14474	1·14470	306	156	141·1	79·8	79·1	1·73	0·01
(VII)	2·2728	1563	1·14450	1·14450	333	183	154·6	98·9	97·4	1·65	0·01
(VIII)	2·2726	1543	1·14609	1·14611	354	219	178·0	120·7	115·8	1·67	0·02
(IX)	2·2727	1760	1·14474	1·14470	301	4	150·4	64·5	67·3	2·05	0·01

(IV) 2 : 5-Dibromoquinol dimethyl ether. (V) 1 : 5-Dimethoxyanthracene. (VI) 9 : 10-Dimethoxyanthracene. (VII) 9 : 10-Dimethoxy-1 : 2-benzanthracene. (VIII) 9 : 10-Dimethoxy-1 : 2-5 : 6-dibenzanthracene. (IX) Hexamethoxybenzene.

The authors thank Professor J. W. Cook, F.R.S., for providing materials, the Department of Scientific and Industrial Research for a Maintenance Allowance (to K. B. E.), and Imperial Chemical Industries Limited for a grant towards the cost of the investigation.

PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, August 3rd*, 1950.]

5. *A Contribution to the Chemistry of the Sesquiterpene Humulene.*

By G. R. Clemo and J. O. Harris.

The sesquiterpene didymocarpene has been identified as humulene. Preliminary degradative experiments on this substance are described which indicate that the compound is monocyclic.

Didymocarpene, the sesquiterpene isolated from the leaves of *Didymocarpus pedicellata* by Warsi and Siddiqui (*J. Indian Chem. Soc.*, 1939, **16**, 423), was described by these authors as yielding a blue nitrosite, m. p. 132—134°. Reinvestigation of this preparation has revealed that two products are formed: a blue mononitrosite, m. p. 115—116°, and a colourless, presumably bisnitrosite, m. p. 165—166°. This is reminiscent of the behaviour of humulene (cf. Chapman, *J.*, 1895, **67**, 780), and identity of these two sesquiterpenes has been established by the preparation of the same nitrosochloride, nitrolpiperidide, and nitroso-derivative from didymocarpene and humulene.

Humulene ($C_{15}H_{24}$), the chief sesquiterpene constituent of hop oil and a minor constituent of the high-boiling terpene fraction of clove oil, has been shown to be present in the essential oil of Egyptian hashish (Simonsen and Todd, *J.*, 1942, 188), and in a variety of Japanese plants (Kohasa, *J. Chem. Soc. Japan*, 1942, **63**, 1483; Fujita, *ibid.*, 1941, **62**, 1014; 1944, **65**, 598; Huzita, *ibid.*, 1939, **60**, 1081; 1940, **61**, 137; 1941, **62**, 134; 424). Hitherto, little degradative work has been performed on it, presumably because of the difficulty of the separation of humulene from the other terpene constituents of these oils. The oil obtained from *Didymocarpus pedicellata* shows good constancy of chemical and physical properties, and we believe that material from this source consists essentially of one substance, and may safely be used for the degradation of this sesquiterpene.

Catalytic hydrogenation over Adams's platinum oxide in acetic acid revealed the presence of three double bonds, which was confirmed by titration with perbenzoic acid. Humulene therefore appears to be monocyclic. Catalytic reduction in alcohol over Adams's platinum oxide at atmospheric pressure reduced only one ethylenic linkage. Attempts to form a maleic anhydride adduct were abortive, and the absence of any conjugated system was confirmed by our inability to reduce the compound with sodium and alcohol. Dehydrogenation gave mainly unchanged material, together with a little azulene coloration. No picrate-yielding product was detected (cf. Simonsen and Todd, *loc. cit.*).

The liquid ozonide obtained in hexane yielded, on decomposition by steam, formaldehyde and lævulaldehyde. More vigorous decomposition of the ozonide with potassium permanganate gave *as*-dimethylsuccinic acid.

Owing to the limited quantities of didymocarpene available, further degradations were performed on the highly crystalline nitrosochloride, easily obtainable from either hop oil or the high-boiling fractions of clove oil. Evans, Ramage, and Simonsen (*J.*, 1934, 1806) described the preparation of nitrosohumulene from this substance, and its subsequent reduction to aminodihydrohumulene. We have catalytically hydrogenated nitrosohumulene to the fully reduced aminohexahydrohumulene, in the hope that subsequent methylation and Hofmann decomposition would yield useful information, but the low yields and scarcity of starting material did not make this an attractive degradative route. We have found, however, that the nitrosochloride can be directly reduced over Raney nickel at 100 atmospheres and 100° to a mixture of isomeric aminotetrahydrohumulene hydrochlorides. This mixture can be separated by trituration with ether into a highly crystalline insoluble α-isomer and an oily uncrystallizable β-isomer. Decomposition of these hydrochlorides yielded the free bases as colourless optically inactive oils. These substances were still unsaturated and both could be reduced further to the fully saturated aminohexahydrohumulenes by prolonged hydrogenation over Adams's platinum oxide in glacial acetic acid. The fully reduced material so obtained from the α-isomer was the same as that obtained by direct reduction of nitrosohumulene in glacial acetic in the presence of Adams's platinum oxide, as shown by the identity of the acetyl derivatives.

The above two primary amines were separately methylated with formaldehyde and formic acid to the corresponding α- and β-dimethylaminotetrahydrohumulenes. These were converted into the crystalline α- and β-tetrahydrohumulene-trimethylammonium iodides which

were decomposed under Hofmann conditions to yield two isomeric hydrocarbons, α- and β-dihydrohumulene, respectively.

Attempts to isolate maleic anhydride adducts from either of those two hydrocarbons were unsuccessful.

α-Dimethylaminotetrahydrohumulene could be hydrogenated further in glacial acetic acid in the presence of Adams's platinum oxide to α-dimethylaminohexahydrohumulene, the quaternary ammonium iodide from which gave on Hofmann degradation a tetrahydrohumulene.

The fact that complete reduction of some of the above substances could only be achieved by hydrogenation in the presence of Adams's platinum oxide, one double bond being resistant to hydrogen over Raney nickel at 100° and 100 atmospheres suggests the presence of an ethylenic linkage between highly alkylated carbon atoms.

Oxidative experiments on these hydrocarbons are in progress.*

Experimental.

The oil obtained by steam-distillation and fractionation of the pedicellin-free filtrate from the ethereal extract of the leaves of *Didymocarpus pedicellata* was redistilled. Almost the whole of the very pale yellow liquid boiled at 74—76°/0·1 mm. and had $n_D^{20\cdot5}$ 1·5003 (Found: C, 87·9; H, 11·6. Calc. for $C_{15}H_{24}$: C, 88·2; H, 11·8%).

Nitrosonitrosite.—Didymocarpene (2·5 g.) in light petroleum (b. p. 40—60°) (2·5 c.c.) was well shaken at 0—5° with saturated sodium nitrite solution (2·5 c.c.). Glacial acetic acid (8·5 c.c.) was slowly added, and shaking continued for 2 hours. A deep blue colour developed, and the blue crystals deposited (0·5 g.) were collected and recrystallized from methanol to yield sky-blue prismatic needles, m. p. 115—116° (decomp.), of a *nitrosonitrosite* (Found: N, 9·9. $C_{15}H_{24}O_3N_2$ requires N, 10·0%). The filtrate, when kept overnight in the refrigerator, deposited very light-yellow needles (0·1 g.) which on recrystallizatiod from light petroleum (b. p. 60—80°) formed colourless needles, m. p. 165—166° (decomp.) (Found: N, 9·8%) (cf. Chapman, *loc. cit.*).

Nitrosochloride.—Didymocarpene (7·0 g.) in a mixture of methylated spirit (15 c.c.), glacial acetic acid (15 c.c.), and ethyl nitrite (7·0 c.c.) was cooled in a freezing-mixture. A well-cooled mixture of glacial acetic acid (7 c.c.) and concentrated hydrochloric acid (7 c.c.) was added with constant stirring. The white precipitate (4·8 g.), after removal and washing with ether, melted at 173—174° (decomp.), not depressed on admixture with humulene nitrosochloride prepared in a similar manner from a sample of hop oil (Chapman, *J.*, 1895, **67**, 54).

Nitroso-derivative.—The above didymocarpene nitrosochloride (4·5 g.) was refluxed with pyridine (6 c.c.) for 5 minutes, and the mixture poured into water and extracted with ether. The ethereal extract was washed (dilute hydrochloric acid), dried (Na_2SO_4), and evaporated, and the residue on distillation yielded a semi-solid mass (bath-temp. 145—155°/1 × 10^{-4} mm.). On recrystallization from aqueous ethanol (80%) it yielded colourless plates, m. p. 128—129°, not depressed on admixture with nitrosohumulene prepared similarly (Evans, Ramage, and Simonsen, *J.*, 1934, 1806).

Nitrolpiperidide.—Didymocarpene nitrosochloride (0·5 g.) and piperidine (3 c.c.) were heated to boiling, and after the rapid reaction had subsided the residue was triturated with a little cold alcohol, the mixture filtered, and the solid recrystallized twice from ethanol. The product (0·2 g.) separated as colourless prisms, m. p. 154—155°, not depressed on admixture with a similar sample prepared from humulene (Chapman, *J.*, 1895, **67**, 780).

Degradation Experiments.—The degradations described for the original sesquiterpene were all performed on the constant-boiling material obtained from the leaves of *Didymocarpus pedicillata* as described above. The starting material for all other experments was the highly crystalline humulene nitrosochloride, obtained from the high-boiling terpene fraction of clove oil in a manner identical with that described by Evans, Ramage, and Simonsen (*loc. cit.*) or from the high-boiling residues of hop oil; these residues (130 c.c.) yielded humulene nitrosochloride (60 g.) (cf. Chapman, *ibid.*, p. 54).

Hydrogenation Experiments.—Humulene (28·9 mg.) in glacial acetic acid (5 c.c.) was hydrogenated in the presence of Adams's platinum oxide (0·1 g.) at atmospheric pressure. Hydrogen uptake was continuous, and practically ceased after 2·8 mols. of hydrogen per mol. of humulene had been absorbed.

Titration of Humulene with Perbenzoic Acid.—Humulene was treated with excess of perbenzoic acid in chloroform, and the solution left in a refrigerator for 6 days. Duplicate determinations of unchanged perbenzoic acid with iodine and thiosulphate indicated the presence of 2·9 double bonds per mol. of humulene.

Attempted Addition of Maleic Anhydride to Humulene.—Humulene (0·5 g.) in benzene (5 c.c.) containing maleic anhydride (0·3 g.) was refluxed overnight. Removal of the solvent and recrystallization of the residue yielded only unchanged maleic anhydride.

Ozonolysis Experiments—Humulene (1·0 g.), dissolved in pure hexane (25 c.c.) and cooled in "Cardice," was ozonized to completion, whereupon a crystalline ozonide separated. The reaction mixture was allowed to warm to room temperature, and the solvent decanted from the tacky ozonide.

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* Since submission of this paper, our attention has been drawn to a communication by Šorm (*Czech. Chem. Comm.*, 1949, **14**, 274) in which we understand the infra-red data on tetrahydrohumulene are discussed. We have examined humulene derivatives twice by the same method during the past three years, but in neither case would our experts commit themselves to any conclusions as to structure.

The latter was distilled in a current of steam, the first 5 c.c. distilling being treated with dimedone solution. The white precipitate produced was crystallized from a small volume of methylated spirit (m. p. alone or mixed with formaldehyde dimedone compound, 189°). The bulk of the steam-distillate was treated with an excess of 2 : 4-dinitrophenylhydrazine hydrochloride solution; a tacky solid separated, which, after trituration with ether and methanol followed by crystallization from dioxan and recrystallization from nitrobenzene, yielded a red micro-crystalline powder, m. p. alone or mixed with lævulaldehyde bis-2 : 4-dinitrophenylhydrazone, 235·5° (Found : C, 44·4; H, 3·5. Calc. for $C_{17}H_{14}O_8N_8$: C, 44·4; H, 3·5%).

A further sample of ozonide (1·0 g.) was refluxed with saturated aqueous potassium permanganate solution (30 c.c.) for 5 hours. The reaction mixture was saturated with sulphur dioxide, acidified (concentrated hydrochloric acid), refluxed for 1 hour, cooled, and extracted with ether in a continuous extractor. The solvent was removed, and the residue extracted with 2N-sodium carbonate. The alkaline solution was removed, acidified, and again extracted with ether. Removal of the solvent yielded a small amount of solid material (*ca.* 10 mg.), m. p. alone, or mixed with an authentic sample of *as*-dimethylsuccinic acid, 137—138° (Found : C, 48·8; H, 6·85. Calc. for $C_6H_{10}O_4$: C, 49·3; H, 6·85%).

Attempted Dehydrogenation of Humulene.—(i) Humulene (1·6 g.) was heated with selenium (2·0 g.) at 280—300° for 40 hours. Some hydrogen selenide was evolved, but unchanged selenium (1·8 g.) was recovered. Distillation of the oil yielded only material which gave no precipitate with picric acid, and after prolonged oxidation with chromic acid on the water-bath, followed by ether extraction, no solid acid material could be isolated. A sample of the recovered oil behaved under catalytic hydrogenation in a manner identical with the starting material. (ii) Attempted dehydrogenation with sulphur at 230—258° for 15 hours, and over palladized charcoal in a furnace at 345—360° at 10 mm., gave similar results.

Catalytic Reduction of Nitrosohumulene.—Nitrosohumulene (1·0 g.), prepared as described by Evans, Ramage, and Simonsen (*loc cit.*), was shaken in glacial acetic acid (30 c.c.) with Adams's platinum oxide (0·1 g.) and hydrogen at 100 lbs./sq. in. for 3 hours. Filtration and removal of solvent yielded a basic liquid, which was converted into its *acetyl* derivative with acetic anhydride. This crystallized from light petroleum (b. p. 40—60°) in colourless needles, m. p. 125—126° (Found : C, 76·8; H, 12·5. $C_{17}H_{33}ON$ requires C, 76·4; H, 12·4%).

Catalytic Reduction of Humulene Nitrosochloride.—Humulene nitrosochloride (44 g.) in methyl alcohol (200 c.c.) was shaken with Raney Nickel (4·0 g.) and hydrogen at 100 atm. and 90—100° for 4 hours. Filtration and removal of solvent yielded a tacky solid; on trituration with ether this gave a highly crystalline *hydrochloride* (16·5 g.) which crystallized from aqueous alcohol in colourless, prismatic needles, m. p. 290—291° (Found : C, 69·7; H, 11·75. $C_{15}H_{29}N,HCl$ requires C, 69·4; H, 11·6%).

The bulk of the above hydrochloride was dissolved in hot water and basified, the oily layer extracted with ether and dried, and the resulting *α-aminotetrahydrohumulene* distilled as an optically inactive, colourless liquid (10 g.), b. p. 76—77°/0·01 mm., n_D^{18} 1·4994 (Found : C, 80·7; H, 12·8. $C_{15}H_{29}N$ requires C, 80·7; H, 13·0%). Quantitative hydrogenation over Adams's platinum oxide in acetic acid revealed the presence of one double bond, and acetylation of the fully reduced base gave an acetyl derivative, m. p. 125°, identical with that obtained by direct hydrogenation of nitrosohumulene.

α-Aminotetrahydrohumulene with acetic anhydride immediately deposited *α-acetamidotetrahydrohumulene* as a white solid which crystallized from light petroleum (b. p. 60—80°) as colourless needles, m. p. 182° (Found : C, 76·7; H, 11·9. $C_{17}H_{31}ON$ requires C, 77·0; H, 11·7%); it decolorized an acetone solution of potassium permanganate only very slowly.

The ethereal solution from the trituration of the above hydrochloride on evaporation yielded an uncrystallizable glass which was easily soluble in water. The aqueous solution on basification yielded an oil which, on extraction, drying, and subsequent distillation, gave *β-aminotetrahydrohumulene* (17·5 g.), optically inactive, b. p. 79°/0·3 mm., n_D^{18} 1·5000 (Found : C, 80·7; H, 12·8%). Attempts to prepare a crystalline hydrochloride, picrate, or acetyl derivative were unsuccessful. Quantitative hydrogenation over Adams's platinum oxide in glacial acetic acid revealed the presence of one double bond.

α-Dimethylaminotetrahydrohumulene.—α-Aminotetrahydrohumulene (18 g.), 40% aqueous formaldehyde (12 c.c.), and formic acid (95%; 12 c.c.) were heated on the steam-bath overnight. The mixture was basified and extracted with ether, and after drying and removal of the solvent, *α-dimethylaminotetrahydrohumulene* was obtained as a colourless oil (18 g.), b. p. 82°/0·3 mm., n_D^{18} 1·4948 (Found : C, 81·0; H, 13·1. $C_{17}H_{33}N$ requires C, 81·2; H, 13·15%).

β-Dimethylaminotetrahydrohumulene.—β-Aminotetrahydrohumulene (48 g.) was treated as above, giving *β-dimethylaminotetrahydrohumulene* (18 g.) as a colourless oil, b. p. 84°/0·3 mm., n_D^{18} 1·4990 (Found : C, 81·2; H, 13·0%).

α-Tetrahydrohumulenetrimethylammonium Iodide.—α-Dimethylaminotetrahydrohumulene (15 g.), in acetone (200 c.c.), was treated with freshly distilled methyl iodide (10 c.c.) and a precipitate was immediately deposited. The reaction mixture was left overnight, and the *α-tetrahydrohumulenetrimethylammonium iodide* (19·5 g.) was filtered off and crystallized from acetone as prismatic needles, m. p. 264° (decomp.) (Found : C, 54·95; H, 9·35. $C_{18}H_{36}NI$ requires C, 55·0; H, 9·2%).

β-Tetrahydrohumulenetrimethylammonium Iodide.—β-Dimethylaminotetrahydrohumulene (28 g.) in acetone (200 c.c.) was treated with methyl iodide (15 c.c.), and the whole left overnight. The solution was concentrated to *ca.* 30 c.c. and allowed to crystallize; *β-tetrahydrohumulenetrimethylammonium iodide* was obtained as needles (26·5 g.) of indistinct m. p. beginning to decompose at 188° (Found : C, 54·8; H, 9·1%).

α-Dihydrohumulene.—α-Tetrahydrohumulenetrimethylammonium iodide (18 g.) was decomposed by being shaken overnight with an excess of freshly precipitated silver oxide (18 g.) suspended in water (200 c.c.). The combined washings and filtrate (250 c.c.) were treated with sodium hydroxide (250 g.); trimethylamine was evolved and an oil separated. The whole was refluxed for 1·5 hours, and the mixture diluted, and extracted with ether. The ethereal solution was washed with dilute acid and water, dried (Na_2SO_4), and evaporated, and the residue distilled from sodium, *α-dihydrohumulene* being obtained as a colourless liquid, b. p. 50°/0·1 mm., n_D^{21} 1·4908 (Found: C, 87·3; H, 12·3. $C_{15}H_{24}$ requires C, 87·4; H, 12·6%). Quantitative hydrogenation over Adams's platinum oxide in acetic acid at room temperature and pressure revealed the presence of two double bonds.

β Dihydrohumulene.—When β-tetrahydrohumulenetrimethylammonium iodide (25 g.) was decomposed and the product worked up as above, *β-dihydrohumulene* (6·6 g.) distilled as a colourless oil, b. p. 53°/0·2 mm., n_D^{21} 1·4960 (Found: C, 87·7; H, 12·3%). Quantitative hydrogenation under the conditions used for the α-isomer again indicated the presence of two double bonds.

Dimethylaminohexahydrohumulene.—α-Dimethylaminotetrahydrohumulene (10 g.) in glacial acetic acid (95 c.c.) was shaken with Adams's platinum oxide (250 mg.) and hydrogenated for 20 hours at atmospheric pressure and room temperature, more catalyst (200 mg.) was added, and the hydrogenation continued for another 30 hours. A third addition of catalyst (150 mg.) was made, and the hydrogenation continued for another 24 hours, reduction then appearing to be complete. The liquid was concentrated and basified and, after extraction of the oil and subsequent distillation, dimethylaminohexahydrohumulene was obtained as a colourless oil (9·1 g.; b. p. 133°/2 mm.).

The above tertiary amine (9·0 g.), acetone (50 c.c.), and methyl iodide (10 c.c.) were mixed and kept for 3 days, and the solvent was then removed; the quaternary *salt* obtained (14·5 g.) recrystallized from a small volume of acetic acid as prisms, m. p. 135—145° (decomp.) (Found: C, 54·7; H, 9·4. $C_{18}H_{34}NI$ requires C, 54·7; H, 9·6%).

This quaternary ammonium iodide (14·0 g.) was decomposed as above, and the hydrocarbon fraction separated and distilled; *tetrahydrohumulene* was obtained as a colourless oil (4·0 g.), b. p. 86°/1 mm. (Found: C, 86·5; H, 13·35. $C_{15}H_{28}$ requires C, 86·5; H, 13·5%). Quantitative catalytic hydrogenation showed the presence of one double bond.

We thank Messrs. White Tomkins & Courage Ltd., and Monsanto Chemicals Ltd., for gifts of hop oil and clove oil terpene, respectively, and Dr. Siddiqui for generous samples of didymocarpene.

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[*Received, September 2nd,* 1950.]

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6. *Chemical Actions of Ionising Radiations in Solution. Part VII. Radiation Chemistry of Sterols. The Action of X-Rays on Cholic Acid in Aqueous Solution.*

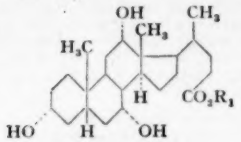
By MAX KELLER and JOSEPH WEISS.

The action of *X*-rays on aqueous solutions of sodium cholate gives, as main product, 3α : 12α-dihydro-7-ketocholanic acid. This substance is also formed in the first stages of the biological oxidation of cholic acid, thus showing again the parallelism between certain biological oxidations and those produced by penetrating radiations in aqueous systems.

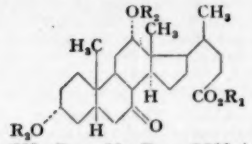
IN previous publications (Parts I—IV, *J.*, 1949, 3241—3263; Parts V and VI, *J.*, 1950, 2704—2714) it has been shown that the action of ionising radiations, *e.g.*, *X*-rays, γ-rays, or neutrons (recoil protons), on dilute aqueous solutions is due to the formation of hydrogen atoms and hydroxyl radicals. In Part VI (*loc. cit.*) we studied the action of *X*-rays on cholesterol and on 3β-hydroxypregn-5-en-20-one in aqueous systems, and found that the hydroxyl radicals attack the double bond in the 5 : 6-position, leading to the formation of the corresponding (*trans*-)triols; in cholesterol, the CH_2 group at $C_{(7)}$ is also attacked, being converted into a keto-group.

In view of the importance of steroid compounds in cell metabolism, we have now extended this study to other sterols, and report the action of *X*-rays on cholic acid (I). An approximately 0·5% aqueous solution of its sodium salt was irradiated with a dose of $\sim 1{\cdot}8 \times 10^6$ r. units of *X*-rays (220 kv.) at about 35°. On elution chromatography after methylation of the crude product with diazomethane, about 80% of the starting material was recovered, and two oily fractions (*a*) and (*b*) were isolated. Fraction (*a*) (~4%) could not be crystallised. Fraction (*b*) (~7%) gave a crystalline product after acetylation which was shown

to be methyl 3 : 12-diacetoxy-7-ketocholanate (III). Hydrolysis of this product gave 3α : 12α-dihydroxy-7-ketocholanic acid (IV), which is therefore the substance originally formed.

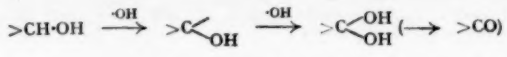


(I; R_1 = H.)
(II; R_1 = Me.)



(III; R_1 = Me, R_2 = COMe.)
(IV; R_1 = R_2 = H.)

The production of this substance by these means is of considerable interest because it has been shown that this keto-acid is also formed as an intermediate in the biological oxidation of cholic acid by *Alcaligenes fæcalis* (Hoehn, Schmidt, and Hughes, *J. Biol. Chem.*, 1944, **152**, 59). This demonstrates—as already shown in Parts I—VI (*locc. cit.*)—that the action of *X*-rays on dilute aqueous solutions is similar to the processes in certain biological oxidations. This observation also sheds further light on the mechanism of the oxidative attack at the 7-position of the sterol structure. It has been suggested (Part VI, *loc. cit.*) that the oxidation of the CH_2 group in this position is a stepwise process proceeding through the intermediate formation of the CH·OH group. In the present case one starts with the CH·OH group and its transformation into the keto-group presumably corresponds to the two (final) stages :



Experimental.

(All m. p.s are uncorrected.)

1 G. of sodium cholate (I) (m. p. 195—196°) in 200 ml. of water was irradiated with a dose of ~$1{\cdot}8 \times 10^6$ r. units of *X*-rays (220 kv.) at about 35°. The irradiated solution was acidified (Congo-red) with hydrochloric acid. The precipitated material was extracted with ether–chloroform, the extract washed with water and dried (Na_2SO_4), and the solvent removed in a vacuum. The residue was methylated with diazomethane in methanol–ether. The solvent was distilled off in a vacuum, the residue dissolved in ether, the extract washed till neutral and dried (Na_2SO_4), and the ether evaporated. The crude ester (about 1 g.) was chromatographed (30 g. of alumina, standardised according to Brockmann). The chromatographic column was prepared in a medium of light petroleum–benzene (1 : 1). Elution with benzene gave an oil (53 mg.), fraction (*a*), which did not crystallise even after acetylation and subsequent hydrolysis. Further elution with ether gave an oil (67 mg.), fraction (*b*). Elution with ether–chloroform mixtures gave methyl cholate (II) (810 mg.), m. p. 110—114°/156—158° (from methanol) (cf. Grand and Reichstein, *Helv. Chim. Acta*, 1945, **28**, 344). Recrystallisation from absolute ether after drying in a vacuum gave a crystalline powder, m. p. 143—144°, not depressed on admixture with an authentic specimen.

Methyl 3α : 12α-*Diacetoxy-7-ketocholanate* (III).—Fraction (*b*) (67 mg.), which did not crystallise, was dissolved in 3 ml. of acetic anhydride and refluxed for 4 hours. The solvent was removed in a vacuum, and the residue dissolved in ether and washed till neutral. After drying, and evaporation of the solvent, the oily residue was crystallised from light petroleum and gave needles (47 mg.), m. p. 115—117° (Gallagher and Long, *J. Biol. Chem.*, 1943, **147**, 131), not depressed in admixture with an authentic specimen of the diacetoxy-ester prepared by methylation and acetylation of the acid made according to Hoehn and Linsk (*J. Amer. Chem. Soc.*, 1945, **67**, 312). For analysis the substance was dried in a high vacuum for 12 hours at 50° (Found : C, 68·9; H, 8·7. Calc. for $C_{29}H_{44}O_7$: C, 69·0; H, 8·8%).

3α : 12α-*Dihydroxy-7-ketocholanic Acid* (IV).—The methyl ester (III) (40 mg.) was heated under reflux with a mixture of 1 ml. of methanol and 1 ml. of 2N-potassium hydroxide for 3 hours. The reaction mixture was diluted with water and acidified with hydrochloric acid. The precipitated crude acid, filtered off and washed with water, had m. p. 86—90° (dried in a desiccator). The acid (IV), when dried for several hours at 120° and crystallised from freshly distilled ethyl acetate, had m. p. 198—200° (6 mg.) (Gallagher and Long, *loc. cit.*; Haslewood, *Biochem. J.*, 1944, **38**, 108), not depressed on admixture with an authentic specimen prepared according to Hoehn and Linsk (*loc. cit.*). For analysis the acid was dried for 12 hours in a high vacuum at 120° (Found : C, 70·5; H, 9·7. Calc. for $C_{24}H_{38}O_5$: C, 70·9; H, 9·4%).

We thank the Medical Research Council for a maintenance grant for one of us (M. K.), and the Northern Council of the British Empire Cancer Campaign for financial support.

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[*Received, September* 16*th*, 1950.]

7. *A Polarographic Study of the Electroreduction of Acridine.*

By R. C. Kaye and H. I. Stonehill.

The reduction of acridine at the dropping-mercury electrode has been studied over the pH range 0—14. In aqueous solution, complex anomalous polarograms are obtained. In solutions containing upwards of 50% alcohol, the anomalies disappear, leaving two one-electron reduction steps which are thermodynamically irreversible, and for which diffusion currents are proportional to acridine concentrations in the range 10^{-3}—10^{-4}M. The anomalies in aqueous solutions may be satisfactorily explained on Brdička's theory as due to adsorption of acridine, mainly in the semiquinone reduced state, on the mercury electrode. Supporting evidence for adsorption has been obtained from a cathode-ray oscillographic study of the current–time relation during the formation of a mercury drop at the electrode. Acridine is found to undergo a two-step electroreduction, both in aqueous and alcoholic solutions, with the formation of an intermediate semiquinone radical, the apparently great stability of which is attributed to resonance.

The behaviour of acridine and some of its derivatives at the dropping-mercury electrode has been studied by Breyer, Buchanan, and Duewell (*J.*, 1944, 360), who concluded that in general these compounds are reduced in two one-electron stages, with the intermediate formation of a semiquinone radical. However, certain anomalies appear in their results. For instance, they describe a three-stage reduction of acridine as well as of 4-aminoacridine; for acridine, the first reduction wave has a constant height for concentrations between 10^{-4}M. and 10^{-3}M., from which they deduce that acridine exists only as a dimer at concentrations exceeding 10^{-4}M. This deduction seems doubtful, since, even if dimerisation did occur, the mass-action law would indicate some increase of wave height with rising concentration. It may be noted that the above workers reported a shift of the half-wave potential of this first reduction step with varying acridine concentration.

These anomalies, and the aim of correlating redox properties of the acridines with their biological activity, have prompted the present investigation.

Experimental.

Acridine was purified by repeated crystallisation from aqueous alcohol, conversion into hydrochloride, recrystallisation from water, drying until water of crystallisation was removed, reconversion into free base, and again crystallisation from aqueous alcohol. The m. p. of the product was 107° (lit., 107°, 110°, 111°). Mercury for the dropping electrode was purified by treatment with potassium permanganate followed by dilute nitric acid, and then vacuum-distilled.

A manually operated polarographic circuit was used. The potential was applied to the cell by means of a potential divider giving steps of 10 mv., and the cell current was measured by a suitably damped Cambridge " Spot " galvanometer calibrated by measuring the voltage drop across a standard resistance in series; this calibration was frequently checked, but no variation was observed. The polarographic cell (Fig. 1), constructed from a B40 Pyrex glass joint, was similar to one described by Kolthoff and Lingane (" Polarography," Interscience Publishers Inc., N.Y., 1946, p. 245). It contained an immersion-type saturated calomel electrode, against which the potential of the dropping-mercury electrode was measured potentiometrically. The hand-drawn Pyrex capillary had the following characteristics: drop time $t = 4{\cdot}2$ secs. with no applied potential; mercury flow rate $m = 0{\cdot}902$ mg./sec. in 50% alcoholic buffer at pH 8·29 (measured in the alcoholic solution).

Solutions in the cell were deoxygenated, before being polarographed, by bubbling through them for 20—30 minutes cylinder nitrogen, purified by passage through a series of wash-bottles containing sodium dithionite solution with a little indigo-carmine redox indicator, to give warning of approaching exhaustion of the dithionite.

Cell solutions were made by dissolving known weights of acridine in known volumes of aqueous supporting electrolyte and diluting them with more of the latter as required; when alcoholic solutions were used, the acridine was dissolved in a suitable volume of absolute alcohol (previously shown to contain no electro-active matter), which was then diluted with aqueous buffer and adjusted to a suitable final volume after mixing and cooling to 25°.

As supporting electrolytes, the following Sörensen buffer solutions, prepared according to Clark (" The Determination of Hydrogen Ions," 1928) were used: pH 1·925 and 3·95, citrate–hydrochloric acid; pH 5·58 and 7·38, phosphate mixtures; pH 9·07, borate–hydrochloric acid; pH 11·0, borate–sodium hydroxide. Some determinations were made with supporting electrolytes containing various percentages of alcohol. For these solutions, the apparent pH values, as determined by a glass-electrode pH meter and checked with a hydrogen electrode, were somewhat higher than those obtained by indicators (cf.

Shreve and Markham, *J. Amer. Chem. Soc.*, 1949, **71**, 2993); the latter values did not differ significantly from the values for the given buffers in purely aqueous solution. All measurements were at 25°, unless otherwise indicated.

To determine the current–time relationships during the life-time of a single drop at the dropping-mercury electrode, an "Ultrascope" Mark I oscilloscope was employed. The polarographic current (max. value about 3 μa.) was amplified by a circuit (Fig. 2) using high-gain valves V_1 and V_2, which both have + 60 v. applied to their screening grids, and small capacities interposed between grid and earth and anode and earth to guard against possible H.F. oscillations in the amplifier. B_1 and B_2 are standard 120-v. high-tension batteries, and potential divider R_3–R_4 is connected across a 48-v. section of B_1. Linear amplification up to about 4 μa. input is obtained by adjusting R_3 until the anode current of V_2 is 0·7 ma., thus achieving the critical setting of the V_2 grid potential necessary to work V_2 near the midpoint of its characteristic curve. Changes in dropping-mercury electrode potential affect the plate current drawn by V_1, thus necessitating resetting the V_2 grid potential by readjusting R_3 and perhaps also the tapping from R_4 on B_1. The amplifier output was fed to the Y plates of the oscilloscope,

FIG. 1.

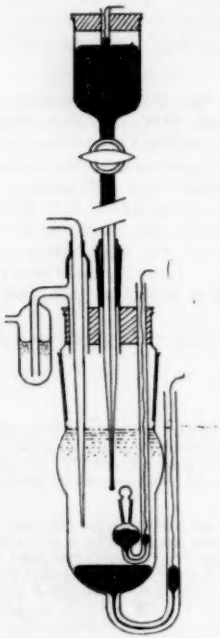
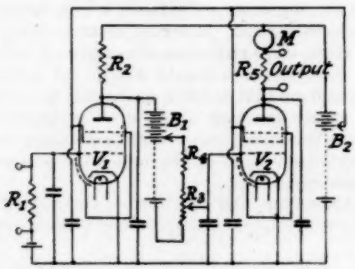


FIG. 2.



R_1, R_3, R_4 = 10,000 *ohms.*
R_2 = 50,000 *ohms.*
R_5 = 100,000 *ohms.*
Capacities of all condensers = 0·001 μF.
V_1, V_2 = EF.50 (Mullard).

whilst to the X plates was connected a 2 μF. condenser which, charged by a 400-v. supply through a 1-megohm series resistance, constituted a simple time base; this, on closing of the circuit, gave a sweep which, although linear over the early portion only, was adequate for the immediate purpose. To photograph an oscillogram, the potential of the dropping-mercury electrode was set at the desired value, the grid potential of V_2 adjusted as described above, and the oscilloscope was then adjusted so that the spot was almost off the left-hand edge of the 6-in. diameter screen, where its periodic vertical deflections, due to the growth and fall of the mercury drops, could still be followed. The shutter of a camera, focused on the screen, was then opened, and the time-base switch closed so that the fall of the mercury drop occurred after the spot had travelled about 1 in. across the screen, *i.e.*, about $\frac{1}{4}$ second after closing the switch; after the spot had completely traversed the screen, the shutter was closed. The delicate timing of the operation was aided by listening to a pocket watch giving 5 ticks per second. Difficulties due to pick-up of 50-cycle mains A.C. ripple in the leads to the amplifier were minimised by screening the leads and earthing the amplifier and oscilloscope. A slight 50-cycle ripple still remained in the oscillogram, but this was deliberately retained, since it provided a useful automatically recorded time scale. The amplifier–oscilloscope combination was simultaneously checked for linearity of amplification and calibrated by applying known constant currents through the 10,000-ohm input resistance, and measuring the vertical displacement of the resulting horizontal linear oscillograms. Linearity was observed up to 3·6 μa. input.

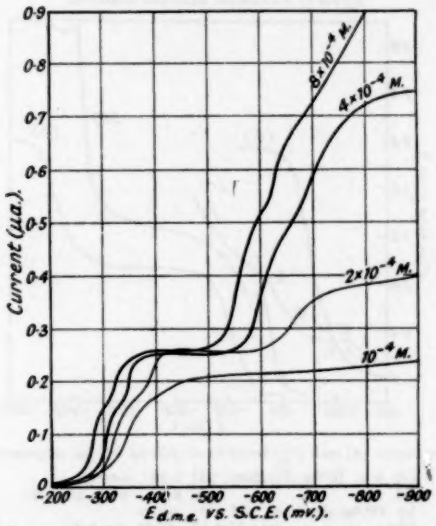
Results and Discussion.

(i) *Evidence for Adsorption as Cause of Anomalies.*—Current–potential polarograms for the reduction of acridine in aqueous solutions at the d.m.e. were obtained at pH values ranging from 0 to 14, and at acridine concentrations in the range 1—8 × 10^{-4}M. Some typical examples are given in Figs. 3 and 4. At pH values above 3 it was necessary to include 5% of alcohol as co-solvent because of the low solubility of the free acridine in water. In general, the polarographic waves are markedly anomalous, and in no case was evidence found to support the general statement made by Breyer, Buchanan, and Duewell (*loc. cit.*) that acridine is reduced in two steps of equal height, although the shift of half-wave potential with change of concentration noted by these workers was confirmed. Multiple waves were of general occurrence and maxima were frequently encountered. Breyer, Buchanan, and Duewell's observation (*loc. cit.*) that the height of the first step remains constant throughout the concentration range 10^{-4}—10^{-3}M. was confirmed for pH values up to 4, but not for higher pH. This constant-height first step is shown in Fig. 3, where it is clear that it apparently consists of two smaller waves.

Inadequate buffering as a possible cause of the anomalous waves was suggested by the work

Fig. 3.

Acridine. pH 1·925; *water.*



Current–potential curves for the reduction of acridine at the dropping-mercury electrode.

of Müller (*J. Amer. Chem. Soc.*, 1940, **62**, 2434), who showed that, when hydrogen ions are involved in electroreductions of organic materials, insufficient buffer may give rise to the appearance of two waves instead of one, as in the case of quinhydrone. However, the anomalies persisted even after greatly increasing the buffer–acridine concentration ratio or in 0·1N-hydrochloric acid supporting electrolyte, thus rendering this explanation of the anomalies improbable.

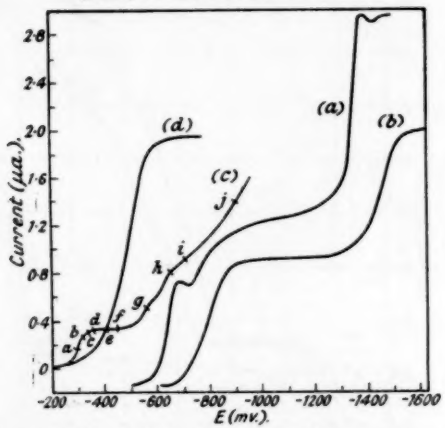
With higher concentrations of acridine, abnormal galvanometer oscillations were observed over a certain range of potentials, despite damping; the current increased very suddenly after the fall of a drop and then *decreased* slowly whilst the drop was still growing. At some dropping-mercury electrode potentials the current passed through several maxima during the life of a drop. We conclude that these effects are due to adsorption of electro-active material on the mercury surface. This conclusion is supported by the work of Albert, Goldacre, and Heyman (*J.*, 1943, 651), who studied the surface activities and partition coefficients of several acridines and found that unsubstituted acridine was the most hydrophobic and surface-active of the compounds examined.

To confirm that adsorption was the cause of the abnormalities, a run was done at pH 6·5 with 4 × 10^{-4}M-acridine in a buffer supporting electrolyte containing 60% (v/v) of alcohol, which was added in order to render the acridine less lyophobic. In the resulting polarogram almost all the

anomalies disappeared; furthermore, the galvanometer oscillations became normal. Further increase of alcohol content to 70% and 75% led to completely normal polarograms. Since, however, such high alcohol contents tended to precipitate buffer salts, and it was desired to examine more closely the effect of varying alcohol content, 0·1N-hydrochloric acid was used as supporting electrolyte. A series of solutions, all containing 0·1N-hydrochloric acid and 4×10^{-4}M-acridine, but with alcohol contents ranging from 5 to 75%, was examined polarographically. The current–voltage curves obtained are reproduced in Fig. 5. Clearly 5% of alcohol is ineffective in preventing adsorption, giving a wave almost identical with that obtained without alcohol (Fig. 3). With increasing alcohol content the waves approach the normal form, reaching this at 60% alcohol. The multiple waves obtained in the absence of alcohol are thus not normal polarographic waves, but are due to adsorption effects. Curves *a* and *b* (Fig. 4) show that at pH 7·38, as also at other pH values, the addition of sufficient alcohol again removes the anomalous multiple waves. Finally, when these anomalous adsorption waves are suppressed by adding alcohol, there is good proportionality between wave-height and acridine concentration, rendering unacceptable Breyer, Buchanan, and Duewell's dimerisation hypothesis (*loc. cit.*), and there is then but a very small shift in half-wave potential with variation in acridine concentration.

FIG. 4.

Effect of alcohol on acridine solutions.



The current scale for curves (a) and (b) should be displaced 0·2 μa. downwards from that shown.

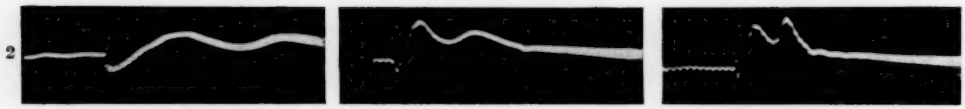
(*a*) 4×10^{-4}M-*Acridine*, pH 7·38; *water.*
(*b*) ,, pH 8·29; 60% *alcohol.*
(*c*) 10^{-3}M-*Acridine*, pH 1·0; *water.*
(*d*) ,, pH 1·17; 60% *alcohol.*

Since the abnormal galvanometer oscillations provided the first indication of adsorption effects, the current–time relationship during the earlier part (*ca.* 2 secs.) of a drop life-time was studied oscillographically in detail (see Experimental). Adsorption effects are likely to be greatest in this period, since the rate of surface increase is greatest when the mercury drop is small. This was confirmed before photographing the oscillograms, by inspecting visually both the early and the late parts of the drop life on the oscilloscope screen, the closing of the time-base switch being suitably delayed for this purpose; adsorption phenomena were confined mainly to the first two seconds of drop life. Fig. 6 (*a* to *l*) reproduces oscillograms showing the current–time relationship at various dropping-mercury electrode potentials for a solution containing 10^{-3}M-acridine in an aqueous buffer at pH 1 (*i.e.*, 0·1N-HCl). It should be studied in conjunction with the correspondingly lettered polarogram (*c*) in Fig. 4. Curve (*a*) represents conditions at the bottom of the polarographic wave, where practically no reduction is occurring, and the current is essentially the residual or condenser current; the current–time relation is almost linear. Curves (*b*), (*c*), and (*d*) refer to the anomalous double adsorption wave in the polarogram (cf. Fig. 3); here the current passes through several maxima during a single drop life. This may possibly be due to adsorption on the growing mercury surface causing temporary blocking of the electrode surface

FIG. 6.

10^{-3}M-*Acridine in water at* pH 1·0.

(*a*) − 299 mv. (*b*) − 321 mv. (*c*) − 338 mv.

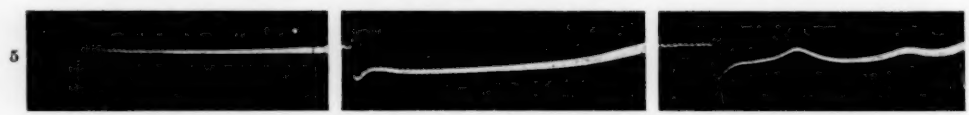


(*d*) − 356 mv. (*e*) − 408 mv. (*f*) − 445 mv.

(*g*) − 558 mv. (*h*) − 646 mv. (*i*) − 708 mv.

(*j*) − 898 mv. (*k*) − 982 mv. (*l*) − 1172 mv.

10^{-3}M-*Acridine in* 50% *alcohol at* pH 1·0.



(*m*) − 398 mv. (*n*) − 447 mv. (*o*) − 528 mv.

(*p*) − 580 mv. (*q*) − 704 mv. (*r*) − 994 mv.

10^{-3}M-*Acridine in* 75% *alcohol at* pH 1·0.

(*s*) − 320 mv. (*t*) − 490 mv. (*u*) − 680 mv.

[*To face p.* 31.

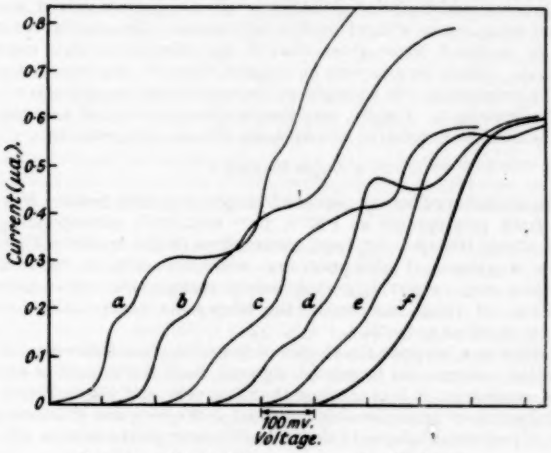
and also a fairly sudden local depletion of electro-active matter in solution, which is made good again by diffusion from the outer bulk solution after a short interval. At oscillogram (*e*) and in subsequent ones, a marked change is observed; immediately after the fall of a drop, the current rises abnormally rapidly, indicating that adsorption here enhances the reduction current. Lastly, at (*l*) the potential is sufficiently negative for hydrogen to be evolved, giving rise to the additional anomalous waves.

Fig. 6 (*m* to *u*) shows oscillograms obtained with the same system but with 50% (*m* to *r*) and 75% (*s* to *u*) of alcohol added. Apparently, 50% of alcohol reduces but does not completely remove the anomalies, while 75% of alcohol entirely eliminates them, permitting normal current-time curves to be obtained.

The adsorption anomalies with acridine in both polarograms and oscillograms are most pronounced in acid solutions; also the adsorption wave has a constant height throughout the concentration range 10^{-4}—10^{-3}M. at pH values up to but not exceeding 4. The pK_a value for acid–base ionisation of acridine is 5·6 in aqueous solution (Albert and Goldacre, *J.*, 1946, 706). This suggests that the acridinium ion rather than the free base is responsible for the anomalies. In support, results obtained with *N*-methylacridinium bromide, which of necessity exists only in the ionic form over the entire pH range, show that strong adsorption at the dropping-mercury

FIG. 5.

Effect of alcohol on 4 × 10^{-4}M.*-acridine at* pH 1·0 (*in water*).



Curve a, 5% *alcohol* *d*, 40 *alcohol*
b, 10 ,, *e*, 47 ,,
c, 30 ,, *f*, 60 ,,

All curves start at −200 mv.

electrode occurs in both acid and alkaline solutions, and is not completely eliminated by high concentrations (75%) of alcohol.

The constant-height adsorption wave previously mentioned resembles strongly the constant-height anomalous fore-waves obtained by Brdička (*Z. Elektrochem.*, 1942, **48**, 278, 656) in the polarographic reduction of methylene-blue and of lactoflavin, which were ascribed to adsorption, confirmed by an oscillographic study. Since the results with lactoflavin are apparently complicated by slow rate-determining processes other than diffusion, we shall restrict our attention to Brdička's work on methylene-blue (*loc. cit.*, p. 278). He points out that, since the fore-wave occurs at potentials more positive than correspond to the main reduction wave, it follows that, the dropping-mercury electrode being treated as an inert-metal redox electrode of potential

$$E = E^{\circ\prime} + (RT/nF) \ln a_{ox.}/a_{red.} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(where $a_{ox.}$, $a_{red.}$ are the activities of oxidised and reduced forms of the organic electro-active material in the interface boundary layer near the mercury drop, and n, $E^{\circ\prime}$, R, T, and F have

their usual significance), either $a_{ox.}$ is greater than, or a_{red} is less than the corresponding values for the bulk solution. The former alternative is inadmissible, but the latter is possible as a result of adsorption of reductant on the mercury, with consequent decrease in free energy. The constancy of height of the fore-wave for concentrations above a minimum and for acid pH values is ascribed to saturation of the mercury surface by adsorption of reductant; only after saturation is complete will an increased applied voltage cause the formation of unadsorbed reductant with an accompanying normal polarographic wave.

The preceding argument based on equation (1) being applied to our own results, it appears that the anomalous fore-waves (Figs. 3 and 5) are due to adsorption of the reduction product from cationic acridine, *i.e.* (since $n = 1$, as shown later), of semiquinone. Further, the distortions at more negative potentials which displace E to more negative values and which are responsible for the new feature appearing in Fig. 6 (*e*—*l*) are due to adsorption of unreduced cationic acridine, which immediately removes electrons from the mercury.

Brdička assumed that the methylene-blue adsorption obeyed the Langmuir isotherm in the form

$$x = abc/(1 + bc) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(where x = amount adsorbed in mol./cm.^{2} at equilibrium concentration c mol./l., a and b being constants). By combining this equation with equation (1) and the Ilkovič equation, he derived an equation giving $E - E^{0/}$ as a function of the (mean) diffusion current $\bar{i}$ and the adsorption current $\bar{i}_a$ (the value of $\bar{i}$ corresponding to the constant-height fore-wave). This last relation gives, with a reasonable choice of values for the constants involved, curves very similar to the experimental polarograms with adsorption fore-waves. By a similar treatment he showed that adsorption of oxidised form gives rise to an adsorption after-wave following the main reduction wave. From the equation he deduced that $E^{0/}$, the true half-wave potential at the given pH, is the potential at the midpoint of the main polarographic wave; this he found to be concentration-independent. Finally, introducing the mean rate of mercury surface growth, he deduced that the maximum value of x in equation (2), *i.e.*, a, is given by

$$a = \bar{i}_a/0{\cdot}85nFm^{\frac{2}{3}}t^{-\frac{1}{6}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where m is the rate of mercury flow in g./sec. and t is the drop time in sec. For methylene-blue, a was evaluated from polarograms as $1{\cdot}62 \times 10^{-12}$ mol./cm.^{2}, corresponding to an area per single molecule of about 100 A.^{2}. Applying these views to our results with acridine, we may conclude, from the occurrence of adsorption fore- and after-waves in the first and the second one-electron reduction step, respectively, that mainly semiquinone is adsorbed at all potentials and over the entire pH-range examined; the adsorption is especially pronounced at low pH (<4) and not too negative potentials.

An important difference between the shapes of the adsorption fore-waves of methylene-blue and of acridine is that, whereas the former are sigmoid, the latter consist of two joined sigmoid portions. In this connection, it is of interest that Peacocke and Hinshelwood (*J.*, 1948, 2290) found that the adsorption of methylene-blue on *Bact. lactis aerogenes* followed a Langmuir type isotherm, but that of proflavine followed a sigmoid isotherm conforming to an equation of the form

$$x = abc^4/(1 + bc^4) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

which is suggested as arising from a co-operative effect due to strong inter-molecular fields, *i.e.*, the presence of adsorbed molecules on given sites facilitates the adsorption of similar molecules on neighbouring sites. It seems reasonable to suppose that equation (4) might apply to the adsorption of acridine on mercury, and to test this hypothesis the relation between E and $\bar{i}$ (potential and polarographic current) was derived graphically with its aid as follows. Assuming a one-electron reduction (see below) and letting ox and s denote the concentrations of acridine and its semiquinone respectively in the boundary layer, we have by the Ilkovič equation

$$ox = (\bar{i}_d - \bar{i})/g \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where $\bar{i}_d$ is the polarographic diffusion current and g is the proportionality factor between concentration (c) and $\bar{i}$ in the Ilkovič equation (*Coll. Czech. Chem. Comm.*, 1934, **6**, 498)

$$\bar{i} = 605nD^{\frac{1}{2}}m^{\frac{2}{3}}t^{\frac{1}{6}}c = ngc \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Following Brdička, $\bar{i}$ is composed of two contributions, one from free semiquinone in the boundary layer, the other from adsorbed semiquinone, giving

$$\bar{i} = gs + \bar{i}_a bs^4/(1 + bs^4) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where adsorption isotherm (4) has been used and $\bar{i}_a$ is the adsorption saturation current. Hence, by equation (1) at 25°, concentrations being used instead of activities,

$$E - E^{0/} = 0{\cdot}0591 \log (\bar{i}_d - \bar{i})/sg \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

With reasonable values $\bar{i}_d = 0{\cdot}75 \times 10^{-6}$ a., $\bar{i}_a = 0{\cdot}25 \times 10^{-6}$ a., $g = 10^{-3}$, $b = 10^{36}$, this last relation may be plotted as $E - E^{0/}$ against $\bar{i}$ if s is evaluated for any given $\bar{i}$ value by interpolation from a plot of $\bar{i}$ against s corresponding to equation (7). The resulting polarogram was in fact very similar to the experimental curves, showing a double sigmoid fore-wave of height $\bar{i}_a$. Another test, in effect the reverse of the foregoing, was to take the experimental polarogram for $\frac{4}{5} \times 10^{-4}$M-acridine at pH 1·925 (Fig. 3), evaluate from it $E^{0/}$ (0·659 v.), $\bar{i}_d$ ($0{\cdot}75 \times 10^{-6}$ a.), $\bar{i}_a$ ($0{\cdot}25 \times 10^{-6}$ a.), and g ($1{\cdot}875 \times 10^{-3}$), and then by equation (8) evaluate s for various points on the adsorption wave and hence calculate the value of $(\bar{i} - gs)/\bar{i}_a$. This represents, following the reasoning upon which equation (7) is based, the current associated with and thus proportional to the adsorption, and a plot of this quantity against s is an adsorption isotherm. As expected, a sigmoid curve was obtained, confirming the approximate validity of (4). From (7) also, values of b were calculated, the fourth-power adsorption law being assumed; these values were not constant, however, ranging from $0{\cdot}6 \times 10^{36}$ to 35×10^{36}, showing that this law is only approximately correct. This is also apparent from the occasionally very complex adsorption waves encountered.

The replacement of the Langmuir isotherm (2) by the fourth-power isotherm (4) does not affect the result (3), which, applied to the polarograms for non-alcoholic solutions at pH 1·925 (Fig. 3, $\bar{i}_a = 0{\cdot}256 \times 10^{-6}$ a.) and pH 1·0 (Fig. 4*c*, $\bar{i}_a = 0{\cdot}277 \times 10^{-6}$ a.), with $m = 0{\cdot}00902$ g./sec., $t = 4{\cdot}2$ secs., gives $a = 1{\cdot}162 \times 10^{-10}$ and $1{\cdot}169 \times 10^{-10}$ mol./cm.^{2}, respectively. Thus, the area occupied per single molecule is $1/6{\cdot}03 \times 10^{23}a$ or 142·8 and 141·8 A.^{2}, respectively (cf. Brdička's result: 100 A.^{2} for methylene-blue). (Structural formulæ indicate that the acridine molecule has a smaller area than that of methylene-blue, *viz.*, approx. 50 A.^{2}.) This result, although expected to be only approximate, is certainly high.

Using abnormal galvanometer oscillations during polarographic reduction as a test, we have found other compounds structurally related to acridine, especially quinoline and methylene-blue, to exhibit adsorption effects. Methylene-blue adsorption was of course noted earlier by Brdička (*loc. cit.*).

(ii) *Semiquinone Formation.*—Breyer, Buchanan, and Duewell (*loc. cit.*) showed, by applying Ilkovič's equation, that in aqueous solutions at 0°, acridine was reduced in two one-electron stages, a semiquinone being the product of the first stage. Now adsorption, by affecting the normal proportionality between current and the one-sixth power of the time during the life of a drop, and also by imposing another factor in addition to the normally exclusive diffusion control of supply of electro-active matter to the d.m.e., may render inapplicable Ilkovič's equation (6); it is thus of interest to re-examine the values of n obtained from this equation. Table I gives values of n calculated for each step in our polarograms for aqueous solutions, equation (6) being used with the appropriate value of t for each half-wave potential, and with $D^{\frac{1}{2}} = 2{\cdot}75 \times 10^{-3}$ (calculated from the value of D at 0° and the temperature coefficient for $\bar{i}_d$ or $D^{\frac{1}{2}}$ as given by Breyer, Buchanan, and Duewell, *loc. cit.*). Where an adsorption fore-wave (or after-wave) occurs, its height has been added to that of the subsequent (or preceding) main wave (cf. Brdička, *loc. cit.*).

As was to be expected from the difficulty in estimating wave heights with any great accuracy, the first and the second step of a given polarogram were only approximately of equal height and $\bar{i}_d$ was only approximately proportional to c. However, on the assumption that only two main waves are present, and the height of any adsorption wave being added to the appropriate main wave, the values of n which result show definitely that two one-electron steps are occurring. A more satisfactory test of the same kind, applied to the experiments in which 50—70% alcohol was present in the solutions, gave the results shown in Table II. Here there is little or no complication due to adsorption waves, and the polarograms consist essentially of two very nearly equal steps, except below pH 5 where the hydrogen wave overlaps the second one, making it unattainable experimentally. The value of D used for these alcoholic solutions was calculated by analogy with Gill's results (Ph.D. Thesis, London, 1947), which show that $D^{\frac{1}{2}}$ decreased by $38 \pm 2\%$ at 25° on addition of 50% alcohol to solutions of anthraquinone-1- and -2-sulphonic acid and 2-hydroxy- and 1 : 2-dihydroxy-anthraquinone, and that for the 2-hydroxy-derivative it was practically constant over the range 50—70% alcohol (cf. Shreve and Markham, *loc. cit.*, who found that $\bar{i}_d$ for *p*-nitroaniline is almost constant for 46—58% alcohol and about 34% lower than in water, and that $D^{\frac{1}{2}}$ is always proportional to $\bar{i}_d$ since $m^{\frac{2}{3}}t^{\frac{1}{6}}$ is practically inde-

TABLE I.

Results for reduction of acridine in aqueous solutions.

		First step.				Second step.				
pH.	c, millimol./l.	$\bar{i}_d$ (μa.).	n.	$-E_a$ (mv.).	$-E_1$ (mv.).	$\bar{i}_d$ (μa.).	n.	$-E_2$ (mv.).	$-E_3$ (mv.).	Remarks.
1·0	0·2	0·4	1·01	344	689	—	—	—	—	Hydrogen wave overlaps 2nd step
	0·4	0·8	1·01	315	650	—	—	—	—	
1·925	0·1	0·2	0·99	351	—	—	—	—	—	
	0·2	0·38	0·96	335	669	—	—	—	—	
	0·4	0·76	0·96	313	660	—	—	—	—	" "
	0·8	1·39	0·88	291	710	—	—	—	—	
3·95	0·2	0·4	1·00	350	680	—	—	—	—	
	0·4	0·74	0·95	340	646	—	—	—	—	" "
5·58	0·1	0·2	1·01	428	—	0·24	1·22	1313	—	
	0·2	0·4	1·01	435	720	0·42	1·07	1320	1435	5% Alcohol added
	0·4	0·7	0·89	470	690	0·78	0·99	1338	1440	
7·38	0·2	0·42	1·06	603	856	0·40	1·01	1329	—	
	0·4	0·71	0·97	637	805	0·80	1·01	1324	—	" "
9·07	0·2	0·42	1·06	765	985	0·36	0·91	1330	—	
	0·4	0·63	0·80	778	950	0·75	0·95	1346	—	" "
11·0	0·1	0·24	1·22	865	1060	0·20	1·01	1330	—	
	0·2	0·42	1·06	905	1147	0·36	0·91	1330	—	" "
	0·4	0·55	0·70	919	1150	0·65	0·82	1333	1440	
13·0	0·1	0·23	1·17	1054	1228	0·20	1·01	1318	—	
	0·2	0·42	1·06	1082	1242	0·42	1·06	1325	1425	" "
	0·4	0·54	0·68	1092	1236	0·70	0·89	1340	1430	

TABLE II.

Results for reduction of acridine in alcoholic solutions.

pH of buffer:			First step.			Second step.			
in H_2O.	with 50% EtOH.	C, millimol./l.	$\bar{i}_d$ (μa.).	n.	$-E_1$ (mv.).	$\bar{i}_d$ (μa.).	n.	$-E_2$ (mv.).	Alcohol, %.
1·0	1·17	0·2	0·27	1·10	430	—	—	—	60
		0·4	0·56	1·14	437	—	—	—	60
		0·8	1·22	1·24	455	—	—	—	60
		0·4	0·60	1·22	455	—	—	—	50
		0·4	0·61	1·24	435	—		—	60
		0·4	0·57	1·19	453	—		—	50
		1·0	1·90	1·54	477	—	—	—	60
1·925	2·36	0·2	0·30	1·22	410	—	—	—	50
3·95	4·81	0·4	0·53	1·07	520	—	—	—	60
5·58	6·51	0·4	0·44	0·90	653	0·60	1·22	1410	50
		0·4	0·50	1·02	695	0·50	1·05	1467	70
		0·4 *	0·38	0·99	718	0·31	0·96	1485	70
7·38	8·29	0·4	0·53	1·07	792	0·53	1·00	1447	55
9·07	10·39	0·4	0·55	1·11	935	0·50	1·04	1428	50
11·0	12·00	0·4	0·54	1·09	1032	0·50	1·04	1457	55
13·0	13·39	0·4	0·55	1·11	1160	0·56	1·17	1425	55

* Temp. 0° c.

pendent of alcohol content or pH). At 25°, we therefore used $D^{\frac{1}{2}} = 1{\cdot}71 \times 10^{-3}$, and at 0°, $D^{\frac{1}{2}} = 1{\cdot}33 \times 10^{-3}$, for 50—70% alcohol. The results, although affected by the uncertainty in D, indicate clearly the existence of two one-electron steps.

In spite of this fact, a graph of E against $\log (\bar{i}_d - \bar{i})/\bar{i}$ for 4×10^{-4}M-acridine in a pH 5·58 buffer containing 70% alcohol, at 25°, although linear, has a slope of 98 mv. for the first step and 66 mv. for the second step, as compared with 59 mv. expected for a reversible one-electron process. With lower alcohol content, *e.g.*, with 8×10^{-4}M-acridine in a buffer at pH 1·0 containing 60% alcohol, the graph is somewhat curved with a slope of about 100 mv. for the first step. Thus the reduction at the d.m.e. is not thermodynamically reversible. It follows that these polarographic potentials cannot be treated strictly as reversible redox potentials, but are more akin to the apparent redox potentials (A.R.P.) of Conant *et al.* (*J. Amer. Chem. Soc.*, 1923, **45**, 1047; 1924, **46**, 1254; 1926, **48**, 2468, 3178; 1930, **52**, 407; *Chem. Reviews*, 1926, **3**, 1). It

is, however, still permissible to attach qualitative significance to values of the semiquinone formation constant K, defined by

$$K = s^2/(\text{red.})(\text{ox.}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

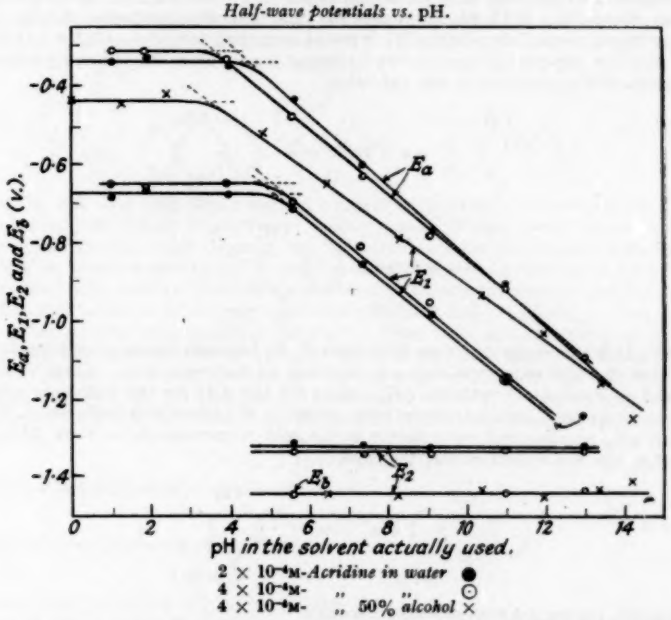
("red." represents the concentration of fully reduced dihydroacridine), when this is calculated by treating the half-wave potentials E_1 and E_2 of the two one-electron steps as if they were reversible potentials, and substituting in the equation (Michaelis, *Ann. N.Y. Acad. Sci.*, 1940, **40**, 39)

$$\sqrt{K} = 10^{E_i/0.0591} - 3 \times 10^{-E_i/0.0591} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where E_i, the index potential, is equal to $\frac{1}{2}(E_1 - E_2)$. Geake's more detailed procedure (*Trans. Faraday Soc.*, 1938, **34**, 1395) for calculating K is inapplicable because of the lack of the necessary symmetry of the polarograms about the midpoint.

FIG. 7.

Half-wave potentials vs. pH.



In order to utilise equation (10), values of E_1 and E_2 for 2 × 10⁻⁴M- and 4 × 10⁻⁴M-acridine in water (Table I) and 4 × 10⁻⁴M-acridine in 50% alcohol (Table II) were plotted against measured pH, as in Fig. 7. For the alcoholic solutions, some data referring to acridine or alcohol concentrations differing slightly from those stated above had to be used; however, Table II shows that this is not likely to cause serious error, since a variation from 45% to 55% alcohol, or from 2 × 10⁻⁴M- to 8 × 10⁻⁴M-acridine, affects E_1 or E_2 by a few centivolts at most. From these plots, smoothed values of E_1 and E_2 were derived by drawing the best-fitting straight lines through experimental points, and these were substituted in equation (10) to give the K values listed in Table III. In most cases, the large values of E_i, due to the great separation of the two reduction waves, rendered the second term of equation (10) negligible in comparison with the first.

These large K values (except at pH 13 in water) indicate that the half-wave potentials E_1 and E_2 approximate closely to the apparent standard redox potentials at any given pH for the two one-electron processes; it is easily shown that the former quantities differ from the latter by $\frac{RT}{F} \ln \left(\sqrt{\frac{3}{K} + \frac{1}{4}} + \frac{1}{2}\right)$ which approaches zero for large values of K. Fig. 7 being interpreted

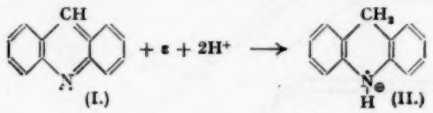
TABLE III.

Values of K *at various* pH *values.*

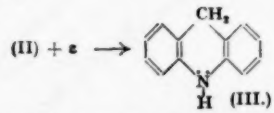
Buffer * pH	In H_2O	3·94	5·58	7·38	9·07	11·04	13·0	14·0
	In 50% EtOH	4·81	6·51	8·29	10·39	12·00	13·39	14·27
E_s (volts)	2×10^{-4}M-Acridine in H_2O	—	0·305	0·237	0·168	0·092	0·044	—
	4×10^{-4}M-Acridine in H_2O	—	0·325	0·252	0·180	0·100	0·052	—
	4×10^{-4}M-Acridine in 50% EtOH	0·457	0·395	0·322	0·262	0·200	0·150	0·120
$\log \sqrt{K}$	2×10^{-4}M-Acridine in H_2O	—	5·16	4·01	2·84	1·56	0·70	—
	4×10^{-4}M-Acridine in H_2O	—	5·50	4·26	3·05	1·69	0·88	—
	4×10^{-4}M-Acridine in 50% EtOH	7·74	6·68	5·45	4·43	3·38	2·60	2·03

* The pairs of pH values above refer to the same buffer mixture in the two different solvents.

on this basis, the zero slope of the graph of E_2 against pH over the accessible pH range indicates that the second reduction step involves no hydrogen ions. On the assumption (cf. Lingane *et al.*, *J. Amer. Chem. Soc.*, 1943, **65**, 1348) that the final reduction product is acridan (III), with two more hydrogen atoms than acridine (I), it would seem that, for pH 5—13 (3·6—13 in alcoholic solutions), the first step should involve two hydrogen ions. Thus the following scheme for the two-stage reduction is plausible in this pH range:

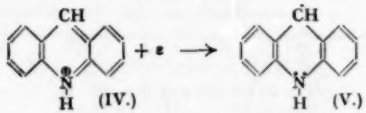


. . . . . (11)



. . . . . (12)

Below about pH 5·1 in water or 3·6 in 50% alcohol, E_1 becomes constant, independent of pH, indicating that the first reduction step now involves no hydrogen ions. These transition pH values accord approximately with the pK_a values 5·6 and 4·11 for the acid–base ionisation of acridine in water and 50% alcohol, respectively, at 20° ± 5° (Albert and Goldacre, *J.*, 1946, 706). At pH below pK_a, acridine will exist mainly in the acid or ammonium ion form (IV). Thus in this pH region, the first reduction step becomes



. . . . . (13)

At such acid pH, the second step probably becomes

$$(V) + \varepsilon + H^+ \longrightarrow (III) \quad . . . . . (14)$$

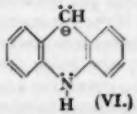
and accordingly the graph of E_2 against pH should have a slope of 0·059 v. per pH unit at pH below pK_a. This is, however, unverifiable, since the hydrogen-deposition wave overlaps the acridine reduction wave at pH below about 5.

There are, nevertheless, objections to the reduction scheme of equations (11) and (12). The E_1–pH graph should, according to equation (11), have a slope of 0·118 v. per pH unit, while the actual slopes are 0·080, 0·084, and 0·071 v. for 2×10^{-4}M-aqueous, 4×10^{-4}M-aqueous, and 4×10^{-4}M-alcoholic (50%) solutions of acridine, respectively, at pH 5—13. These slopes are closer to the value of 0·059 v. for a step involving only one hydrogen ion, the remaining discrepancy being ascribable to the irreversibility of the reduction; alcohol–water junction potentials apparently reduce the discrepancy. Further, it is unlikely that the semiquinone would exist in the cationic or acidic form (II) at pH above 5 (equation 11), and in the non-ionic or basic form (V) at more acid pH values (equation 13); the reverse behaviour would be expected if the semiquinone could undergo acid–base dissociation in this way. In fact, there is no evidence of such dissociation, since this would cause a fairly sharp decrease in the slope of the E_1–pH curve or increase in the slope of the E_2–pH curve when the pH rose above pK_a, where K_a is the

hypothetical acid constant of the semiquinone; neither effect is observed. In view of these objections, the following alternative reduction scheme may be proposed for pH above 5 in water or 3·6 in 50% alcohol:

$$(I) + \varepsilon + H^+ \longrightarrow (V) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

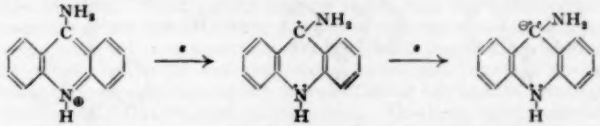
$$(V) + \varepsilon \longrightarrow$$



(VI.) . . . . . (16)

Support for this scheme is provided by some results (to be published) which we have obtained for the polarographic reduction of 5-aminoacridine; this gives two one-electron reduction steps, the half-wave potentials of which are both independent of pH over a considerable alkaline range lying below pK_a for the unreduced substance, indicating that the latter when mainly in the cationic form (VII) undergoes the following two-stage reduction not involving hydrogen ions, and gives an anionic product (VIII) similar to (VI):

(VII.)



(VIII.)

Substances (V) and (VI) might be expected to react with unreduced acridine (see below) and abstract a proton from water, respectively; such processes, if slow, could explain the irreversibility of the two reduction steps (15) and (16). Processes similar to (16), not involving hydrogen ions, and leading to substances like (VI) which probably take up a proton from a water molecule to form a neutral final product, have been postulated for the second of two one-electron reduction steps of phenolphthalein in its red quinonoid form (Kolthoff and Lehmicke, *J. Amer. Chem. Soc.*, 1948, **70**, 1879), of 8-hydroxyquinoline (Stock, *J.*, 1949, 586), of cinchonic acid (Casimir and Lyons, *J.*, 1950, 783), and possibly of quinoline-8-carboxylic acid (Stock, *J.*, 1949, 763).

Let T, T^+ denote the un-ionised and the ionised form of acridine, respectively, and S the sole form of semiquinone (V) postulated in equations (13)—(16). For a reversible process corresponding to equation (15), with standard redox potential E°_{15}, the redox potential (in v.) at 25° is given by

$$E = E^\circ_{15} - 0{\cdot}059 \log [S]/[T][H^+] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (17)$$

For the ionisation equilibrium of acridine we have

$$[T^+] = [T][H^+]/K_a$$

and for the total concentration of unreduced acridine

$$[Ox] = [T] + [T^+] = [T]\{1 + [H^+]/K_a\}$$

Substituting for [T] in terms of [Ox] in equation (17), we have

$$E = E^\circ_{15} + 0{\cdot}059 \log K_a - 0{\cdot}059 \log [S]/[Ox] - 0{\cdot}059 \log ([H^+] + K_a)/[H^+]$$

At the half-wave potential for reduction (15), [Ox] = [S] and $E = E_1$, so

$$E_1 = E^\circ_{15} + 0{\cdot}059 \log K_a - 0{\cdot}059 \log ([H^+] + K_a)/[H^+] \quad . \quad . \quad . \quad . \quad (18)$$

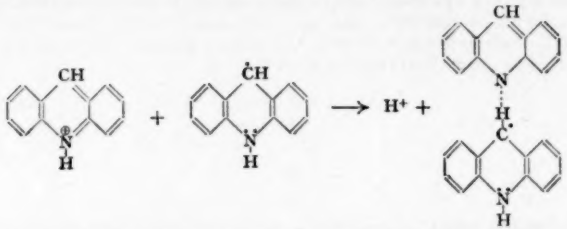
If this treatment had been based on equation (13), the same result would have been obtained except that E°_{13} would replace $E^\circ_{15} + 0{\cdot}059 \log K_a$. That these are equal follows from a consideration of the free-energy changes in (13), (15), and the ionisation of acridine. With a suitable choice of values for E°_{13} and K_a (*e.g.*, −0·435 v. and $10^{-3\cdot6}$ respectively for 50% alcoholic solutions), equation (18) when plotted as E_1 against pH reproduces the experimental curve (Fig. 7) fairly well, except that the slope of the inclined portion is 0·059 v. A similar treatment based on equation (11), the sole form of semiquinone assumed to be (II), leads to

$$E_1 = E^\circ_{11} + 0{\cdot}059 \log K_a - 0{\cdot}059 \log ([H^+] + K_a)/[H^+]^2$$

which gives an E_1–pH graph consisting of two inclined portions, one at pH below pK_a with slope 0·059 v., the other above pK_a with slope 0·118 v., contrary to the experimental results.

In Table I are given values of the half-wave potentials E_a and E_b for the adsorption fore-wave of the first reduction step and the adsorption after-wave of the second step, respectively. These

are plotted against pH in Fig. 7. The E_a–pH curve closely resembles the E_1–pH curve, with a zero slope portion at low pH and a one-hydrogen-ion slope at higher pH, indicating that the fame reduction processes (13) and (15) occur over the potential regions corresponding to the sore-wave and the first main reduction wave. Similarly, the E_b–pH and E_2–pH graphs both have zero slope. However, the transition pH between zero and non-zero slopes is lower for E_a (4·5 and 3·7 for 2×10^{-4}M. and 4×10^{-4}M., respectively) than for E_1 (5·1). This indicates that adsorption of semiquinone has in some way lowered the effective pK_a of unreduced acridine. A possible mechanism, suggested by the large area occupied by each semiquinone molecule at adsorption saturation and by the co-operative adsorption isotherm which applies approximately, is interaction of acridine with semiquinone to release a hydrogen ion from the former, whereupon the two molecules may link by hydrogen bonding; the net effect is co-adsorption of acridine with semiquinone, together with enhanced acid ionisation of the acridine :



The high apparent K values in Table III suggest that the semiquinone (V) has a great stability against disproportionation into acridine and acridan. This stability is enhanced by adding alcohol to the solvent (cf. Burstein and Davidson, *Trans. Electrochem. Soc.*, 1941, **80**, 175), in keeping with the non-ionic nature of (V). It may be ascribed to resonance among various structures in which the odd electron may be situated as in (V), or in either of the benzene rings in positions ortho or para to the point of attachment to the nitrogen atom; allowing for Kekulé benzene-ring resonance, there are thus 16 contributory structures, as compared with only 4 each, due to Kekulé resonance, for acridine and acridan.

The authors thank Principal H. Richardson of Bradford Technical College for his encouragement of this work, and Dr. R. Gill for helpful discussions.

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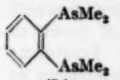
8. *Studies in Co-ordination Chemistry. Part VII. Complexes of Univalent Copper with a (Ditertiary Arsine).*

By A. Kabesh and R. S. Nyholm.

The complexes formed by univalent copper salts with the di(tertiary arsine) chelate group, *o*-phenylenebisdimethylarsine, have been investigated. Co-ordination compounds have been isolated of the empirical formulæ CuX,2(Diarsine) and CuX,(Diarsine), where X = Cl, Br, and I. Compounds of the first type are more soluble in alcohol than those of the second type; they form electrolytically conducting solutions in nitrobenzene and give rise to a perchlorate of the formula $[Cu(Diarsine)_2]ClO_4$; whence it is concluded that they are salts of four-covalent copper of the type $[Cu(Diarsine)_2]X$. Compounds of the second type are considered to be salts also, with the formula $[Cu(Diarsine)_2][CuX_2]$, and evidence in support of this formulation rather than a halogen-bridge structure is presented. All these cuprous complexes are diamagnetic. Attempts to prepare compounds in which the di(tertiary arsine) was co-ordinated to a cupric atom were unsuccessful.

In earlier papers in this series (Nyholm, *J.*, 1950, 851, 857, 2061, 2071), the stereochemistry of the complex compounds formed by the chelate group *o*-phenylenebisdimethylarsine (I) with

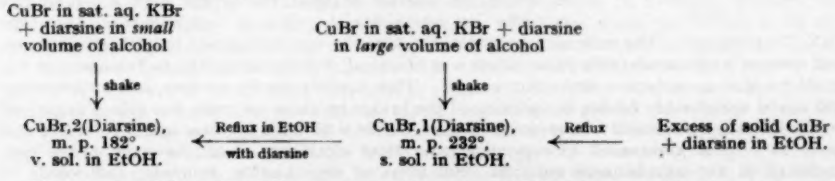
iron, rhodium, nickel, and cobalt halides was investigated. Several of these showed marked stability, with strong covalent bonds, and since stabilisation of the higher valency state was observed in certain cases it was decided to study the behaviour of this chelate group with copper. Much work has been done on the complexes of copper with tertiary arsines but none has been reported on those with tertiary arsine chelate groups. Mann and Purdie (*J.*, 1936, 1503) described complexes of univalent copper with trialkyl-arsines and -phosphines and proved that tetramers of the type $[CuI,AsEt_3]_4$ were formed. The crystal structure of the triethylarsine compound was studied by Wells (*Z. Krist.*, 1937, **94**, 447), who showed that each cuprous atom was tetrahedrally co-ordinated; in addition to one covalently bound iodine atom, each copper atom was attached to two other iodine atoms, presumably by a co-ordinate link, and the triethylarsine molecule completed the four-fold co-ordination. The molecular weights of these compounds in various organic solvents showed four-fold association Using methyldiphenylarsine and dimethylphenylarsine, Burrows and Sandford (*J. Proc. Roy. Soc. N.S.W.*, 1935, **69**, 182) isolated compounds with the formulæ CuX,AsR_2R' and $CuX,2AsR_2R'$, where X = Cl, Br, I, and NO_3. They found that several compounds of the type CuX,AsR_2R' were monomeric in freezing benzene solution. These results suggest either that the compounds are tetramers which are considerably dissociated, or that the copper is two-covalent. The molecular complexity of the compounds with two molecules of arsine to each copper atom was not investigated. A co-ordination number of two for univalent copper is unusual but there is other evidence to show that univalent copper may behave like univalent silver and gold in this respect (Sidgwick, "The Chemical Elements." Oxford, 1950, p. 143 *et seq.*). However, apart from the *X*-ray crystal structure determination of cuprous oxide (Niggli, *Z. Krist.*, 1922, **57**, 253; see also Wells, "Structural Inorganic Chemistry," Oxford, 1945, p. 505), the evidence for a co-ordination number of two for univalent copper in crystalline compounds is slight.



(I.)

No cupric complexes of tertiary arsines were described by Mann and his co-workers, but Burrows and Sandford (*loc. cit.*) described two isomeric cupric–cuprous complexes to which the formula $Cu_2Cl_3,3AsPh_2Me$ was ascribed. Halogen-bridge structures were suggested by Mellor, Burrows, and Morris (*Nature*, 1938, **141**, 414) to account for the isomerism, but the formulæ were difficult to establish with finality. As shown later, the ease with which bivalent copper is reduced by *tert.*-arsines makes it rather unlikely that the arsine is co-ordinated to the cupric atom and the latter is possibly present as a cuprichloride ion. The formulation of these isomers and the structures of other cuprous complexes of methyldiphenylarsine are being investigated. In the present investigation no cupric complexes with *o*-phenylenebisdimethylarsine were obtained; oxidation usually led to perhalides or complexes of indefinite composition.

The chelate group used here co-ordinated so readily with univalent copper that preparation of the compounds was carried out simply by shaking an aqueous solution of the cuprous halide, dissolved in excess of the corresponding potassium halide, with the required amount of the chelating compound dissolved in alcohol. The reaction was very much affected by the amount of alcohol used: a very small amount gave CuBr,2(Diarsine) and CuI,2(Diarsine), but a considerable amount afforded CuBr,(Diarsine) and CuI,(Diarsine). The chloride, CuCl,(Diarsine), was prepared in like manner, but isolation of CuCl,2(Diarsine) was difficult owing to its high solubility in aqueous alcohol; furthermore, it decomposed readily when washed with alcohol or water, giving the di(tertiary arsine) and cuprous chloride. The preparation of a compound of the type CuX,(Diarsine) (where X = halogen) may be effected also by refluxing an alcoholic solution of the di(tertiary arsine) with excess of the cuprous halide, the required compound crystallising out on cooling. This method of preparation was particularly suited to the preparation of the compound CuI,(Diarsine). The relationships between the two types of compound are illustrated by reference to the two bromides:


CuBr in sat. aq. KBr + diarsine in small volume of alcohol
shake
CuBr,2(Diarsine), m. p. 182°, v. sol. in EtOH.
Reflux in EtOH with diarsine
CuBr in sat. aq. KBr + diarsine in large volume of alcohol
shake
CuBr,1(Diarsine), m. p. 232°, s. sol. in EtOH.
Reflux
Excess of solid CuBr + diarsine in EtOH.

The structural formulæ of these compounds were established by a combination of chemical and physical methods. It seemed likely that the compounds containing two molecules of

the chelate group were salts of the type $[Cu(Diarsine)_2]Br$. Treatment of an aqueous-alcoholic or acetone solution of these compounds with silver nitrate gave a precipitate of silver bromide or iodide instantly, followed by a black precipitate of silver owing to reduction of excess of silver ion by the cuprous complex. This suggested that the halogen was ionised. Treatment of an aqueous-alcoholic solution of the complexes with perchloric acid gave a compound of the formula $[Cu(Diarsine)_2]ClO_4$ at once. Confirmation of the salt-like character of these compounds is provided by their molecular weights and conductivities in nitrobenzene solution. The molecular weights observed are a little over half the formula weight, which is the result expected for almost complete dissociation into two ions. The molecular weights in benzene and chloroform will be discussed later. The conductivities of the bromide, iodide, and perchlorate in nitrobenzene solution were next measured, and these showed that ions were present. In the following table are shown the molecular conductivities (Λ) of several of the compounds investigated at concentrations of M/100 or less in nitrobenzene solution. For the bromide, iodide, and perchlorate the molecular conductivity is about 20—30 mho, and values similar to these have been observed by other workers for the molecular conductivities of uni-univalent electrolytes in nitrobenzene; *e.g.*, Foss and Gibson (*J.*, 1950, 3063) found that di-2-pyridyldiethylgold(III) dibromodiethylaurate(III), *i.e.*, $[dipy,AuEt_2][AuEt_2Br_2]$, a uni-univalent electrolyte, had a molecular conductivity which varied between 26·7 and 24·6 mhos for concentrations between 0·0002 and 0·0028M.

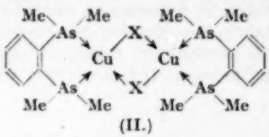
Molecular conductivities of cuprous complexes in nitrobenzene at 25°.

Compound.	M. p.	Concn., M.	Λ, mhos.
$[Cu(Diarsine)_2]I$	189°	0·0092	23·3
$[Cu(Diarsine)_2]Br$	182	0·0070	24·3
,,	—	0·00175	28·5
$[Cu(Diarsine)_2][ClO_4]$	>300 *	0·0069	28·1
$[Cu(Diarsine)_2][CuCl_2]$	266	0·00663	29·4
$[Cu(Diarsine)_2][CuBr_2]$	232	0·00463	28·8
$[Cu(Diarsine)_2][CuI_2]$	174	0·0054	17·9

* Decomposes.

It is evident, therefore, that these compounds are salts in which the four-covalent cuprous atom is co-ordinated to four arsenic atoms. The solubilities of the bromide and iodide, however, call for comment: both dissolved very easily in cold chloroform and are appreciably soluble in hot benzene. Their solubility must be ascribed to the presence of a very large cation containing many organic groups which apparently enables the compound to dissolve with the anion attached. These compounds are similar in this respect to the tetra-alkylammonium halides, certain of which are soluble in chloroform and benzene in which they must dissolve as ion-pairs. The molecular weights of both the iodide and the bromide were measured in boiling chloroform and values a little less than the formula weight were obtained. This also suggests the formation of ion-pairs.

Compounds of the type $CuX,(Diarsine)$ can be formulated in two obvious ways—as salts of the type $[Cu(Diarsine)_2][CuX_2]$, or halogen-bridged dimers of type (II). The halogen-bridge hypothesis, although apparently favoured in view of the ease with which such association occurs in $[CuI,AsEt_3]_4$, was not supported by the properties of these compounds and was abandoned in favour of the alternative structure for the following reasons. If these compounds had the bridged structure (II) one would expect to observe the following properties: (i) a molecular weight in suitable solvents corresponding to twice the formula weight of $CuX,(Diarsine)$; (ii) no electrolytic conductivity in nitrobenzene solution; (iii) it should be possible to split the bridge with a ligand like pyridine or *p*-toluidine to give a compound of the type $CuX,(Diarsine),py$. The molecular weight of the chloride was determined in both nitrobenzene and acetone and considerable dissociation was observed, but the solubility in benzene was too small to give an accurate molecular weight. This dissociation in acetone and nitrobenzene still might conceivably be due to splitting of the bridge by these solvents, but this is negatived by the fact that treatment of a solution of the chloride with both pyridine and *p*-toluidine still gave the original compound on concentration. Most significant of all, however, is the conductivity of the nitrobenzene solution. Solutions of the chloride, bromide, and iodide in nitrobenzene at about 0·005M-concentration all showed molecular conductivities of about 20—30 mhos, indicating two ions (see table). It should be pointed out that the molecular-



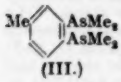
(II.)

weight measurements and the conductivity measurements on these compounds only indicate that in the solvent the solute is present as $[Cu(Diarsine)_2][CuX_2]$ and do not establish with certainty that the compounds are not bridged in the solid state. However, it is considered improbable that a change from the bridged to the salt-like structure occurs on dissolution, as it would involve migration of a molecule of the chelate group. Furthermore, none of the properties of these substances suggests that the bridged structure is correct. It was observed that, in all solvents, compounds of the type $[Cu(Diarsine)_2][CuX_2]$ were less soluble than those of the type $[Cu(Diarsine)_2]X$, a phenomenon apparently associated with the larger anion. A chemical proof that the same action is present in both types of compound is provided by the fact that acetone solutions of both give the same perchlorate, $[Cu(Diarsine)_2]ClO_4$, on treatment with perchloric acid. The bromide being taken as an example, the two compounds would be [di-(*o*-phenylenebisdimethylarsine)copper(I)] bromide and dibromocuprite(I).

This and previous work emphasises that care must be taken before assigning halogen-bridged structures to co-ordination complexes. Mann and his co-workers (*J.*, 1936, 873; 1938, 702; 1940, 1209; see also *Ann. Reports*, 1938, **35**, 148) have demonstrated conclusively that such bridges occur in the tertiary arsine and phosphine complexes of palladium, mercury, and cadmium, and Chatt (*J.*, 1950, 2301) has shown that bridges are present in platinum complexes of the type $[PtX_2,PR_3]_2$. Their use, however, with some other metals simply to complete the usual co-ordination number needs to be proved before being accepted. Recently, Foss and Gibson (*loc. cit.*) showed that certain gold complexes, for which bridged structures were originally proposed, were in fact salts. The presence of large organic groups in the molecules of tertiary arsines and phosphines frequently confers upon a complex solubility in organic solvents which may give the impression that it is a non-electrolyte. In particular, solubility in nitrobenzene must not be taken as indicating that the compound is a non-electrolyte; in Part III (*J.*, 1950, 851) it was shown that ferric complexes of the formula $FeCl_3$,(Diarsine), which were initially thought to be halogen-bridged dimers of octahedrally co-ordinated ferric iron, were in fact salts of the type $[FeCl_2,(Diarsine)_2][FeCl_4]$. This compound was very soluble in nitrobenzene but was highly dissociated in it. Other reported cases where co-ordination complexes believed to be salts have been formulated as non-electrolytes on the basis of their solubility in organic solvents, are being investigated.

Attempts to obtain cupric complexes with this chelate group, either of the type $[Cu(Diarsine)_2]X_2$ or $[CuX_2,(Diarsine)]$ (X = univalent anion) have been unsuccessful. When chlorine is added to the compound $[Cu(Diarsine)_2][CuCl_2]$ in chloroform solution, the halogen is absorbed readily but the product is of indefinite composition and the manner in which it gradually undergoes change in moist air suggests partial oxidation of the diarsine initially. Addition of bromine to a solution of $(Cu(Diarsine)_2]Br$ gave a purple compound which dissolved in both acetone and nitrobenzene to a green solution. It appeared to contain the cupribromide ion but again its indefinite composition made investigation unprofitable. Addition of iodine to the compound $[Cu(Diarsine)_2]I$ in chloroform solution gave a yellow crystalline compound which, after recrystallisation from benzene, melted at 155°. Like the monoiodide, this compound was still diamagnetic, showing that bivalent copper was not present. Analysis showed this substance to be very roughly of composition $Cu(Diarsine)_2I_3$ and it seemed probable that the two extra iodine atoms were present as an I_3^- ion or had been used to effect partial oxidation of the tertiary arsine. Of the two hypotheses, the former seemed the more likely, but since the compound obviously did not contain bivalent copper, the substance was not further investigated. Attempts to prepare the cupric compound $[Cu(Diarsine)_2][ClO_4]_2$ were also unsuccessful. When a cold solution of copper sulphate in aqueous alcoholic perchloric acid was treated with a cold alcoholic solution of the di(tertiary arsine), a brown colour was observed at first but, within a second, spontaneous reduction occurred to give the white crystalline cuprous compound $[Cu(Diarsine)_2]ClO_4$. Finally, treatment of the di(tertiary arsine) in alcoholic solution with cupric chloride directly failed to give a compound in which the arsine was co-ordinated to a cupric atom; especially on heating, reduction to form a cuprous complex occurred.

This investigation shows that, whereas iron, cobalt, and nickel were stabilised in their higher valency states with this chelate group, copper on the other hand co-ordinates only in its lower valency state. In this respect, arsenic is somewhat similar to sulphur which also seems preferentially to stabilise the univalent state. The investigation produced no evidence concerning the stereochemistry of these complexes. No doubt the copper atom is tetrahedral, and the diamagnetism is consistent with the use of sp^3 tetrahedral bonds, but this has not been proved for these compounds. It is noteworthy that no case has yet been reported of the resolution of a complex



(III.)

of univalent copper. The stability of the compounds of the type $[Cu(Diarsine)_2]Br$ (or I), suggests that by using an unsymmetrical chelate group such as (III), it might be possible to achieve the optical resolution of a tetrahedral cuprous complex. This is being further examined.

Experimental.

[*Di*-(o-*phenylenebisdimethylarsine*)*copper*(I)] *Dichlorocuprite*(I).—Cuprous chloride (1·5 g.) was dissolved in saturated aqueous potassium chloride solution (50 ml.) containing 1 drop of 10N-hydrochloric acid and the solution was filtered. The filtrate was treated with *o*-phenylenebisdimethylarsine (4·0 g.) in absolute alcohol (6 ml.) and well shaken for 10 minutes in a stoppered flask. A white crystalline precipitate was formed at once and after ½ hour and occasional shaking the solution was filtered and the compound washed many times with saturated potassium chloride solution and dried at the pump. (Washing with water or alcohol at this stage was liable to cause decomposition.) The dry mixture of the complex and potassium chloride was extracted with chloroform in small amounts (total volume 150 ml.), and the chloroform solution filtered and treated with excess of light petroleum (b. p. 60—80°). The white crystalline compound was filtered off and well washed with light petroleum (4·4 g.). After recrystallisation from either acetone or alcohol the *salt* melted at 266° [Found: C, 31·4; H, 4·3; Cl, 9·2%; *M* (ebullioscopic in acetone; 2·73% solution), 405; (cryoscopic in nitrobenzene, 2·03% solution, 448; (4·64% solution), 454). $C_{20}H_{32}Cl_2As_4Cu_2$ requires: C, 31·2; H, 4·16; Cl, 9·2%; *M*, 770]. The compound was very soluble in chloroform, bromoform, and nitrobenzene, soluble in acetone and hot alcohol, and slightly soluble in benzene; it was insoluble in water and light petroleum. Treatment of an acetone solution of the complex with aqueous silver nitrate gave a precipitate of silver chloride at once, followed by reduction of excess of silver nitrate to silver. In powder form, the compound was diamagnetic with $\chi = -0{\cdot}43 \times 10^{-6}$ at 16·5°. For conductivity in nitrobenzene, see the table. When treated with excess of 30% aqueous perchloric acid, an acetone solution of the compound afforded a precipitate of the perchlorate $[Cu(Diarsine)_2]ClO_4$.

[*Di*-(o-*phenylenebisdimethylarsine*)*copper*(I)] *Bromide*.—Cuprous bromide (1·5 g.) was dissolved in a saturated aqueous solution of potassium bromide (30 ml.) containing concentrated hydrobromic acid (1 drop), and the solution filtered at once into a stoppered flask. To this was added *o*-phenylenebisdimethylarsine (2·9 g.) dissolved in alcohol (10 ml.). A white precipitate was formed immediately and after the mixture had been shaken for ½ hour was filtered off and washed three times with saturated potassium bromide solution and thrice with distilled water. The *bromide* was too soluble in alcohol to permit of recrystallisation from this solvent, so it was purified by recrystallisation from a mixture of chloroform and light petroleum and obtained as a white crystalline powder (2·7 g.), m. p. 182° [Found: C, 33·6; H, 4·7; Br, 11·2%; *M* (ebullioscopic in acetone; 3·5% solution), 410; (4·2% solution), 430; (in chloroform; 2·5% solution), 632; (cryoscopic in nitrobenzene, 2·92% solution), 435; (4·95% solution), 452. $C_{20}H_{32}As_4BrCu$ requires C, 33·6; H, 4·48; Br, 11·2%; *M*, 715·5]. The compound was very soluble in chloroform, bromoform, nitrobenzene, alcohol, and acetone, and slightly soluble in benzene, but insoluble in water. An alcoholic solution reacted instantly with silver nitrate solution to give a precipitate of silver bromide followed by silver. In powder form, the compound was diamagnetic with $\chi = -0{\cdot}50 \times 10^{-6}$ at 23°. For conductivity in nitrobenzene, see table.

[*Di*-(o-*phenylenebisdimethylarsine*)*copper*(I)] *Dibromocuprite*(I).—By a procedure similar to the foregoing [CuBr (1·0 g.), warm saturated aqueous KBr (30 ml.), hydrobromic acid (1 drop), *o*-phenylenebisdimethylarsine (1·5 g.), alcohol (90 ml.)] a white precipitate was obtained immediately, and after ½ hour's shaking and standing overnight, the *dibromocuprite* was collected, washed once with aqueous alcohol (50%) then with saturated aqueous potassium bromide solution, and finally with water to remove potassium bromide. After recrystallisation from alcohol the compound (1·8 g.) melted at 232° (Found: C, 28·1; H, 3·8; Br, 18·7. $C_{20}H_{32}As_4Br_2Cu_2$ requires C, 27·9; H, 3·7; Br, 18·6%); it was very soluble in chloroform, bromoform, and nitrobenzene, and dissolved in acetone and hot alcohol, but was only slightly soluble in benzene. It was insoluble in water and light petroleum. It was diamagnetic, but the exact susceptibility was not determined. For electrolytic conductivity in nitrobenzene solution, see table.

[*Di*-(o-*phenylenebisdimethylarsine*)*copper*(I) *Iodide*.—By the foregoing procedure [CuI (1·9 g.), saturated aqueous KI solution (50 ml.), *o*-phenylenebisdimethylarsine (2·8 g.) in absolute alcohol (5 ml.)], a white precipitate was formed at once, and after 5 minutes' shaking and ½ hour's standing, the *iodide* was collected and well washed with saturated potassium iodide solution followed by distilled water and finally with aqueous alcohol. It was then recrystallised from alcohol and dried in a vacuum desiccator; yield 2·0 g., m. p. 189° [Found: C, 31·8; H, 4·3; I, 16·6; Cu, 8·6%; *M* (ebullioscopic in benzene; 3·1% solution), 660; (in chloroform; 2·5% solution), 750. $C_{20}H_{32}As_4ICu$ requires C, 31·4; H, 4·2; I, 16·6; Cu, 8·3%; *M*, 762·6]. The compound was very soluble in chloroform, soluble in acetone, and moderately soluble in alcohol, and dissolved in hot benzene. On treatment with silver nitrate, it behaved analogously to the bromide. In powder form the compound was diamagnetic with $\chi = -0{\cdot}53 \times 10^{-6}$ at 20·6°. For conductivity in nitrobenzene, see table.

[*Di*-(o-*phenylenebisdimethylarsine*)*copper*(I)] *Di-iodocuprite*(I).—Cuprous iodide (0·7 g.) was heated under reflux with alcohol (50 ml.) containing *o*-phenylenebisdimethylarsine (1·0 g.) for about ¾ hour. Most of the cuprous iodide, which was present in excess, dissolved, but a dark suspension gradually formed, presumably owing to partial reduction of the cuprous iodide by the tertiary arsine. The solution was then filtered hot, and the clear filtrate on cooling gave sparkling plates of the *di-iodocuprite* (0·9 g.), m. p. 174° (Found: C, 25·5; H, 3·4; I, 26·7; Cu, 13·5. $C_{20}H_{32}As_4I_2Cu_2$ requires C, 25·2; H, 3·36; I, 26·7; Cu, 13·34%). The compound had solubilities similar to those of its chloro- and bromo-analogues, and its behaviour with silver nitrate was similar. In spite of the fair solubility in

benzene at room temperature, the low solubility at the freezing point vitiated attempts to determine the molecular weight cryoscopically. For conductivity in nitrobenzene, see table. This compound may also be obtained by treatment of a solution of cuprous iodide in saturated aqueous potassium iodide with an alcoholic solution of the di(tertiary arsine). The product contains some of the monoiodide which must be separated by treatment with hot alcohol, in which it is more soluble than the required product. The method given above is, however, preferable.

[*Di*-(o-*phenylenebisdimethylarsine*)*copper*(I)] *Perchlorate.*—(i) The monobromide (0·6 g.), dissolved in absolute alcohol (50 ml.), was treated with 60% perchloric acid (10 ml.), and the solution well stirred; a white precipitate was obtained immediately, and was filtered off and washed many times with alcohol and dried in a vacuum desiccator; yield 0·4 g. It decomposed explosively when heated to 310° (Found: C, 32·6; H, 4·5; Cu, 8·5. $C_{20}H_{22}O_4ClAs_4Cu$ requires C, 32·7; H, 4·4; Cu, 8·6%). When it was heated with silver nitrate and nitric acid no silver chloride was formed, showing that all the halogen was present as perchlorate. The compound was insoluble in water and in organic solvents other than nitrobenzene.

(ii) Copper sulphate pentahydrate (0·65 g.) was dissolved in distilled water (17 ml.) containing 60% perchloric acid (5 ml.), and the solution filtered. To the cold solution was added o-phenylenebisdimethylarsine (1·45 g.) dissolved in alcohol (40 ml.). A red brown colour was observed momentarily on mixing but this quickly gave place to a white precipitate. The mixture was well shaken for ½ hour, then filtered, and the compound well washed with alcohol. The *perchlorate* (1·3 g.) was obtained as pearly white plates [Found: C, 33·0; H, 4·0; Cl (by Carius method), 5·2. $C_{20}H_{22}O_4ClAs_4Cu$ requires C, 32·7; H, 4·4; Cl, 4·8%], having properties identical with those of the compound prepared as in (i). In powder form, the compound was diamagnetic, with $\chi = -0{\cdot}46 \times 10^{-6}$ at 17°. For conductivity in nitrobenzene, see table.

Action of Iodine on the Iodide.—The monoiodide [Cu(Diarsine)$_2$]I (1·9 g.) was dissolved in chloroform (15 ml.), and iodine (0·5 g.) dissolved in chloroform (10 ml.) added. The solution became brownish-purple and the chloroform was then removed at the pump, giving a yellowish-brown residue which when recrystallised rapidly from alcohol, gave a brownish-yellow compound (1·36 g.), m. p. 152° (Found: C, 24·5; H, 3·2; I, 32·0. Calc. for $C_{28}N_{32}As_4I_2Cu$: C, 23·7; H, 3·16; I, 37·6%). This compound was diamagnetic ($\chi = -0{\cdot}42 \times 10^{-6}$ at 15°) and hence did not contain bivalent copper. The mother-liquors from the above recrystallisation deposited excess of the monoiodide. The compound was then recrystallised from benzene and obtained as sparkling golden-brown plates (0·5 g.), m. p. 155° (Found: C, 24·6; H, 3·9; I, 34·7%). The analysis is still not that of the tri-iodide, [Cu(Diarsine)$_2$]I$_3$ as above, probably owing to contamination with the monoiodide. Since oxidation to bivalent copper has not occurred, the extra iodine has apparently either oxidised part of the arsenic or is present as a tri-iodide ion.

Electrolytic Conductivities in Nitrobenzene.—The nitrobenzene was purified by fractional crystallisation, followed by drying (P_2O_5) and distillation under reduced pressure. Its specific conductivity was $0{\cdot}73 \times 10^{-8}$ mho/cm.^{3}. A dip-type conductivity cell was used, of constant 0·515. The electrodes were of bright platinum and unplated. All measurements were carried out at 25° in a thermostat.

Analysis.—Microanalyses for carbon and hydrogen, also chlorine by the Carius method, were carried out by Messrs Weiler and Strauss, Oxford. For halogen and copper, about 0·2 g. of the compound was treated with excess of silver nitrate (20 ml. of M/20-solution), distilled water (20 ml.), and 15N-nitric acid (30 ml.), and the mixture heated on the water-bath. The black precipitate of silver dissolved rapidly, and heating was then continued until decomposition was complete (about 3 hours). The silver halide was then filtered off and weighed in a sintered Gooch crucible in the usual manner. The filtrate was used for the copper determination. Excess of silver ion was precipitated as chloride, coagulated, and filtered off. The solution was then made alkaline with sodium hydroxide, just acidified with acetic acid, cooled, and treated with a slight excess of salicylaldoxime solution (1 g. in 5 ml. of absolute alcohol + 95 ml. of distilled water). The precipitated copper complex was filtered off after ½ hour, dried at 105°, and weighed. The copper determination was checked by carrying out a Kjeldahl decomposition with concentrated sulphuric acid and potassium sulphate on one of the compounds, and the reliability of the above procedure was established.

The authors are indebted to Professor E. D. Hughes, F.R.S., and Dr. R. G. Wilkins for helpful criticism and to Professor C. K. Ingold, F.R.S., for his continued interest. The award by the University of London of an Imperial Chemical Industries Fellowship to one of them (R. S. N.), during the tenure of which this work was carried out, is also gratefully acknowledged.

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9. *Researches on Acetylenic Compounds. Part XXVIII. A New Route to Diacetylene and its Symmetrical Derivatives.*

By J. B. Armitage, E. R. H. Jones, and M. C. Whiting.

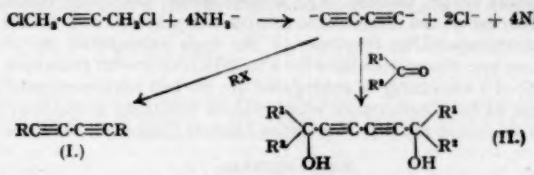
Treatment of the readily available 1 : 4-dichlorobut-2-yne with aqueous sodium hydroxide gives diacetylene in good yield. When the dehydrohalogenation is effected with sodamide in liquid ammonia the disodium salt can be prepared, and this can then react *in situ* with alkyl halides or with carbonyl compounds to give symmetrical conjugated diacetylenic hydrocarbons or glycols.

Although diacetylene has been known for many years (Baeyer, *Ber.*, 1885, **18**, 674, 2269) and although its potential applications in organic synthesis are numerous and important, its widespread use has been precluded by the difficulty of preparing it in quantity. Many methods of synthesis have been investigated. Baeyer (*loc. cit.*) obtained it by decarboxylation of the corresponding dicarboxylic acid; Zalkind and Aizikovich (*J. Gen. Chem. Russia*, 1937, **7**, 227; *Chem. Abs.*, 1937, **31**, 4283) observed its formation in the alkaline decomposition of 2 : 7-dimethylocta-3 : 5-diyne-2 : 7-diol. Numerous examples of its formation in very small yields in pyrolytic decompositions have been recorded, and its isolation from the by-product of the arc process for acetylene synthesis, as operated just before and during the war in Germany (see Copenhaver and Bigelow, " Acetylene and Carbon Monoxide Chemistry," Reinhold, New York, 1949, p. 300), probably made possible the only well-known instance of its use on a comparatively large scale (Kuhn and Wallenfels, *Ber.*, 1938, **71**, 1889). The most useful techniques for the laboratory preparation of diacetylene hitherto described, however, have involved the oxidation of metallic derivatives of acetylene. That of Strauss and Kolleck (*Ber.*, 1926, **59**, 1664), employing cupric chloride and cuprous acetylide, has furnished the small quantities necessary for several physical investigations whilst very recently Schlubach and Wolf (*Annalen*, 1950, **568**, 141) have described an elegant method whereby sodium acetylide is oxidised by potassium permanganate in liquid ammonia, giving a 35% yield of diacetylene.

Amongst the methods previously employed, the only route which appeared to offer possibilities of development into a convenient synthesis for use on a moderately large scale was that discovered by Keyssner and Eichler (G.P., 740,637; *Chem. Abs.*, 1946, **40**, 586) and confirmed by Johnson (*J.*, 1946, 1009). This involves treatment of 1 : 4-dichlorobut-2-yne—easily prepared from the corresponding glycol, which is now commercially available—with " alkaline reagents." Our investigations have shown that the nature of the alkaline reagent is critical; thus with potassium hydroxide in ethanol or 2-ethoxyethanol, reaction occurred at room temperature, but the solvent retained diacetylene so strongly that its removal, before subsequent alkali-catalysed addition of alcohol to give a 1-alkoxybut-1-en-3-yne (see Copenhaver and Bigelow, *op. cit.*, p. 305; Johnson, *loc. cit.*), proved impracticable. On stirring the chloride with aqueous alkalis it was found that calcium hydroxide, potassium carbonate, and trisodium phosphate failed to give any diacetylene even at 100°, whilst 10% sodium hydroxide gave a good (60%) yield. When stronger solutions of sodium hydroxide were used more polymeric material was formed and the yield fell; on the other hand, the addition of 10% of dioxan proved beneficial. Diacetylene was readily isolated in a graduated trap at −25°. Although it has not as yet been necessary to prepare more than 15 g. in one experiment, there seems no reason to doubt that many times this quantity could be obtained without difficulty. Numerous experiments involving the preparation and redistillation of diacetylene have been carried out without mishap, but it should be remembered that potentially this is a dangerously explosive substance (see Copenhaver and Bigelow, *op. cit.*, p. 303). Diacetylene rapidly decomposes at temperatures near its boiling-point, giving explosive polymers, and for that reason it was invariably kept at −25° or below until used. It was characterised by condensation with acetone through its Grignard derivative, whereby the crystalline 2 : 7-dimethylocta-3 : 5-diyne-2 : 7-diol was obtained in 62% yield.

When 1 : 4-dichlorobut-2-yne was treated with sodamide in liquid ammonia rapid dehydrohalogenation ensued; indeed when after one minute the excess of sodamide was decomposed by ammonium nitrate, and the ammonia evaporated, titration of the resulting sodium chloride showed that at least 95% of the theoretical quantity had been formed. A control experiment in the absence of sodamide showed that no appreciable liberation of chloride ions from 1 : 4-dichlorobut-2-yne occurs in 30 minutes (*cf.* Johnson, *loc. cit.*). When four molecular proportions of

sodamide were employed the disodium salt of diacetylene was apparently formed, since addition of methyl iodide then gave dimethyldiacetylene (hexa-2 : 4-diyne) in 65% yield.



This crystalline hydrocarbon has been the subject of much investigation; previous work is reviewed by Schlubach and Wolf (*loc. cit.*). Its preparation on a scale of about 20 g. by the present procedure involved no difficulties other than those inherent in its physical properties; it has m. p. 67° and b. p. 129° and is so volatile that purification by recrystallisation was deemed impracticable. On the other hand, distillation at 760 mm. or 100 mm., on a fairly large scale, resulted in explosive decomposition; but sublimation, with the apparatus illustrated, proved convenient.

The preparation of octa-3 : 5-diyne (I; R = Et) and of dodeca-5 : 7-diyne (I; R = Bu) by the action of ethyl iodide and butyl bromide, respectively, on disodiodiacetylene in about 50% yield, indicates that this reaction is general for primary aliphatic halides. On the other hand, the use of benzyl chloride and of 2 : 4-dinitrochlorobenzene gave only intractable tars. When allyl bromide was used, there was obtained a 25% yield of an approximately homogeneous liquid which certainly was not the expected deca-1 : 9-diene-4 : 6-diyne (I; R = CH_2=CH·CH_2) since it showed light-absorption maxima at 2300 and 2800 A., $E^{1\%}_{1cm.}$ = 830 and 55, and formed an insoluble silver derivative. In view of the instability of the compound, and of the known complexity of the reactions between allyl halides and sodium acetylide (Lespieau and Journaud, *Bull. Soc. chim.*, 1931, **49**, 423; see also Eglinton and Whiting, *J.*, 1950, 3650) further investigations were not attempted.

When the solution of disodiodiacetylene was treated with carbonyl compounds, diacetylenic glycols of type (II) were obtained. In the case of aliphatic ketones (including pinacone) the yields are excellent (86—93%); methyl nonyl ketone alone gave less satisfactory results (yield 36%). Aliphatic aldehydes (formaldehyde, acetaldehyde, and butyraldehyde) also gave good yields (60—90%), but a longer reaction period was needed and the results were more adversely affected by the presence of water in the liquid ammonia (*cf.* Clapperton and McGregor, *J. Amer. Chem. Soc.*, 1949, **71**, 3234). Aromatic ketones also gave good (~50%) yields after a long reaction period when the reaction was carried out in a 1 : 3 mixture of ether and liquid ammonia; but benzaldehyde gave only a 7% yield of the corresponding glycol, which was not improved by working at −70°, substituting lithium or calcium for sodium, or wide variations in reaction time and in the ratio of the reactants. In most of these cases the glycols were known substances and had melting points in agreement with literature values. The present method is complementary to that involving oxidative coupling of ethynylcarbinols, and is in general preferable for small-scale experiments and in cases where the latter are difficultly accessible, *e.g.*, for the glycols derived from formaldehyde and acetophenone.

Attempts to extend this reaction to αβ-unsaturated aldehydes (acraldehyde and crotonaldehyde) were uniformly unsuccessful, only polymeric materials being obtained despite wide variations in reaction conditions. Three αβ-unsaturated ketones were investigated; mesityl oxide gave only the ammonia-adduct, diacetoneamine, β-ionone was recovered unchanged in 84% yield after a 24-hour reaction-period, and benzylideneacetone gave a 50% yield of a syrup which is believed, from physical properties and analytical and spectrographic data, to have consisted essentially of the expected glycol (II; R_1 = Ph·CH=CH, R_2 = Me). Kuhn and Wallenfells (*loc. cit.*) described this as a crystalline solid, but here, as with all glycols from unsymmetrical carbonyl compounds, the formation of a mixture of *meso*- and racemic forms is to be expected.

Attempts to induce disodiodiacetylene to react with ethylene oxide, propylene oxide, and epichlorohydrin proved unsuccessful. It is clear that there is no close parallel between the reactions of sodium acetylide and the derivative of diacetylene; the most conspicuous difference is observed in the reactions with acetophenone, when the latter gives a much higher yield (60%, as against 20%) in a shorter time, and with benzaldehyde, where the yields are 7% and *ca.* 80%, respectively. The explanation may lie in the greater acid strength of diacetylene, which on the

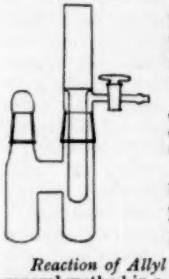
one hand implies reduced reactivity of its anion as a nucleophilic reagent toward somewhat inert carbonyl compounds, *e.g.*, β-ionone, and on the other diminishes its tendency to react with readily enolisable, and therefore acidic, ketones, (*e.g.*, acetophenone) merely by proton transfer. The light-absorption properties of the diacetylenic compounds prepared will be discussed in a later publication. Dehydrohalogenation reactions of the type exemplified by the conversion of 1 : 4-dichlorobut-2-yne into diacetylene have been found to occur with great ease, and have made possible the synthesis of a wide range of conjugated di-, tri- and tetra-acetylenic compounds, the preparation and some of the properties of which will be described in the near future. A brief account of this work was given recently in a Tilden Lecture (Jones, *J.*, 1950, 754).

Experimental.

Diacetylene.—A mixture of 1 : 4-dichlorobut-2-yne (6·1 g.), potassium hydroxide (6 g.), water (60 c.c.), and dioxan (6 c.c.) was stirred vigorously and heated under reflux. The gas evolved, after passing up the reflux condenser, was led over calcium chloride and into a graduated trap at −25°. Diacetylene collected as a liquid (1·5 g.; 60%) which readily crystallised as well-formed plates on cooling to −70°. It was transferred slowly by means of a stream of nitrogen into a solution of ethylmagnesium bromide, prepared from magnesium (1·6 g.), in dry ether (60 c.c.). The solution thus obtained was stirred for 30 minutes, acetone (3·48 g.) was slowly added with cooling, and the solution was refluxed for one hour. Isolation of the product gave a pale-yellow solid (3·4 g.) which was crystallised from water to give 2 : 7-dimethylocta-3 : 5-diyne-2 : 7-diol (3·1 g.; 62%) as needles, m. p. 129° (Strauss, Kollek, and Hauptmann, *Ber.*, 1930, **63**, 1886, give m. p. 129—130°).

Disubstituted Diacetylenes.—General method. To a suspension of sodamide prepared without mechanical stirring in a small vacuum flask from liquid ammonia (100 c.c.), sodium (4·6 g.), and ferric nitrate (0·05 g.) by the procedure described by Vaughn, Vogt, and Nieuwland (*J. Amer. Chem. Soc.*, 1934, **56**, 2120), 1 : 4-dichlorobut-2-yne (6·1 g.) was added slowly with shaking. After one minute the second reactant was added, and the mixture was set aside for some time. Ammonium chloride (12 g.) was added and the contents of the flask were transferred to a beaker; after the ammonia had largely evaporated the residue was repeatedly extracted with ether, and the product was isolated by crystallisation or distillation.

Hexa-2 : 4-diyne. This hydrocarbon was prepared essentially by the general method but on a much larger scale in a 3-l. vacuum flask from sodium (37 g.), 1 : 4-dichlorobut-2-yne (49 g.), and methyl iodide (114 g.); the reaction period was three hours. The crude product was isolated with ether, and the ether removed through a 50-cm. Fenske column. The pale-brown residual solid was sublimed in four portions, the apparatus shown being used, at 30° (bath temp.)/9 mm., to give the pure hydrocarbon (20 g.; 65%) as prisms, m. p. 67° (Prévost, *Ann. Chim.*, 1928, **10**, 372, gives m. p. 64·5°, b. p. 129°; Schlubach and Wolf, *Annalen*, 1950, **568**, 141, give m. p. 68·5°).



Octa-3 : 5-diyne. The reaction was carried out by the general method by using ethyl iodide (15·6 g.) with a reaction period of three hours. The crude product was distilled to give octa-3 : 5-diyne (2·3 g.; 43%), b. p. 69°/17 mm., n_D^{23} 1·4928 (Dupont, *Compt. rend.*, 1909, **148**, 1522, gives b. p. 163—164°, n_D 1·4968).

Dodeca-5 : 7-diyne. The reaction was carried out by the general method by using butyl bromide (13·7 g.) with a reaction period of 19 hours. The crude product was distilled to give dodeca-5 : 7-diyne (4·0 g.; 50%), b. p. 83°/0·5 mm., n_D^{18} 1·4920. The use of butyl iodide gave a similar yield of product (Grignard and Tcheoufaki, *Compt. rend.*, 1929, **188**, 358, give b. p. 103°/8 mm.)

Reaction of Allyl Bromide with Disodiodiacetylene.—The reaction was carried out essentially by the general method in a 1·5-l. vacuum vessel by using sodium (18·4 g.), 1 : 4-dichlorobut-2-yne (24·6 g.), and allyl bromide (48·4 g.); the reaction period was three hours. The crude product was distilled to give a liquid (5·2 g.), b. p. 38°/0·02 mm., n_D^{20} 1·5176 (Found: C, 91·5; H, 8·5. $C_{10}H_{10}$ requires C, 92·3; H, 7·7%). *Active hydrogen* (Zerewitinoff). The product (5·54 mg.) evolved 0·49 c.c. of methane at 20°/766·4 mm., corresponding to 0·5 active hydrogen atom per $C_{10}H_{10}$ unit.

Hydrogenation. The product (0·707 g.) in ethyl alcohol (50 c.c.) was shaken in hydrogen in the presence of platinic oxide (Adams) catalyst (10 mg.) until absorption was complete (uptake 648 c.c. at 23°/765 mm.; 5 moles of hydrogen per mole of $C_{10}H_{10}$).

Hexa-2 : 4-diyne-1 : 6-diol.—The reaction was carried out essentially by the general method but on a 1-molar scale, in a 3 l.-vacuum vessel by using sodium (92 g.), ferric nitrate (1 g.), 1 : 4-dichlorobut-2-yne (123 g.), and paraformaldehyde (60 g.; dried over concentrated sulphuric acid) with a reaction period of 24 hours. The crude product, isolated as a pale-yellow solid (102 g.; 93%), had m. p. 110—112° and was therefore already fairly pure; a portion (5·1 g.) was recrystallised from ethyl acetate–light petroleum (b. p. 80—100°) to give the pure glycol (4·85 g., equivalent to 88% yield) as plates, m. p. 112°. Alternatively, sublimation at 80° (bath temp.)/10^{-4} mm. gave the glycol, m. p. 112° (Lespieau, *Ann. Chim.*, 1897, **11**, 232, gives m. p. 111—112°).

Octa-3 : 5-diyne-2 : 7-diol.—The reaction was carried out by the general method by using acetaldehyde (4·4 g.) in dry ether (50 c.c.) with a reaction period of 24 hours. Isolation of the product gave a solid (6·2 g.; 89%), m. p. 83—85°, which was recrystallised from benzene to give the almost colourless pure glycol (4·9 g.; 71%), m. p. 85—86°. Alternatively, sublimation at 80° (bath temp.)/10^{-5} mm. gave the glycol as long rectangular plates, m. p. 85—86°. (Zalkind and Gverdsiteli, *J. Gen. Chem. Russia*, 1939, **9**, 971, give m. p. 108—109° for one of the stereoisomeric forms. The other has m. p. 67·5—68°

according to Lespieau, *Ann. chim.*, 1912, **27**, 137.) When the reaction period was reduced to two hours the yield of glycol after crystallisation from benzene, was 0·7 g. (10%).

Dodeca-5 : 7-diyne-4 : 8-diol.—The reaction was carried out by the general method by using butyraldehyde (7·2 g.) in dry ether (50 c.c.) with a reaction time of 24 hours. Distillation of the crude product gave the glycol (6·5 g.) as a viscous liquid, b. p. 147°/0·5 mm., n_D^{20} 1·5170 (Bowden, Heilbron, Jones, and Sargent, *J.*, 1947, 1581, give b. p. 138°/10^{-4} mm., $n_D^{18\cdot5}$ 1·5175).

1 : 6-Diphenylhexa-2 : 4-diyne-1 : 6-diol.—The reaction was carried out by the general method by using benzaldehyde (10·6 g.) with a reaction time of one hour. The crude product was a deep-red, very viscous liquid which partially crystallised. Trituration with benzene gave a light-brown solid (0·9 g.), m. p. 127—130°, which after crystallisation from benzene formed needles, m. p. 131—133° (Kuhn and Wallenfells, *loc. cit.*, give m. p.s 81—85° and 131—132·5° for the two stereoisomeric forms). Chromatography of the residue failed to give more crystalline material, and the use of reaction periods of five minutes and of 24 hours, and of 1½ hours at −70° led to the formation of uncrystallisable dark syrups. When lithium (1·4 g.) was used in place of sodium with a reaction period of 15 minutes the yield of glycol, m. p. 133° (recrystallised), was 0·8 g.

2 : 7-Dimethylocta-3 : 5-diyne-2 : 7-diol.—The reaction was carried out by the general method by using acetone (5·8 g.) with a reaction period of 60 minutes. Isolation of the crude product gave a solid (8·2 g.; 97%), m. p. 126—128°, which was sublimed at 90° (bath temp.)/10^{-4} mm. to give the pure glycol (7·5 g.; 87%) as long needles, m. p. 129°. Recrystallisation from water, the small amount of tarry impurity being removed by filtration, was an equally satisfactory method of purification (Strauss, Kolleck, and Hauptmann, *loc. cit.*, give m. p. 129—130°). When the reaction period was reduced to five minutes the yield of crude glycol was 83%.

3 : 8-Dimethyldeca-4 : 6-diyne-3 : 8-diol.—The reaction was carried out by the general method by using methyl ethyl ketone (7·2 g.) with a reaction period of three hours. Isolation of the crude product gave a solid (9 g.; 93%), m. p. 83—88°, which after crystallisation from ethyl acetate–light petroleum (b. p. 80—100°) gave the pure glycol (8·5 g.) as small prisms, m. p. 89°. The crude glycol could also be purified by sublimation at 100° (bath temp.)/10^{-4} mm. (I.G. Farben., G.P. 765,469, give m. p. 89°).

10 : 15-Dimethyltetracosa-11 : 13-diyne-10 : 15-diol.—The reaction was carried out by the general method by using methyl nonyl ketone (17 g.) with a reaction period of 24 hours. Isolation of the crude product gave a dark-red viscous liquid (10 g.) which was distilled to give the pure glycol (7 g.; 36%), b. p. 150° (bath temp.)/10^{-4} mm., m. p. 45—46° (Bowden, Heilbron, Jones, and Sargent, *loc. cit.*, give b. p. 210°/10^{-3} mm., m. p. 40—43°).

2 : 2 : 3 : 8 : 9 : 9-Hexamethyldeca-4 : 6-diyne-3 : 8-diol.—The reaction was carried out by the general method by using pinacone (10 g.) with a reaction period of three hours. Isolation of the crude glycol gave a pale-yellow solid (12·5 g.), m. p. 248—252°, which was recrystallised from aqueous methanol to give the *monohydrate* (12 g.; 90%) as needles (Found, in a sample dried at 20° in a desiccator: C, 71·45; H, 10·85. $C_{14}H_{26}O_2,H_2O$ requires C, 71·6; H, 10·5%). On being heated above 100° or dried at 50°/10^{-4} mm. the monohydrate was decomposed giving the anhydrous *glycol*, m. p. 248—251°, which when cool rapidly absorbed moisture from the air (Found: C, 76·8; H, 10·7. $C_{14}H_{26}O_2$ requires C, 76·8; H, 10·5%).

Di-(1-hydroxycyclohexyl)buta-1 : 3-diyne.—The reaction was carried out by the general method by using *cyclo*hexanone (9·8 g.) with a reaction time of one hour. The product was isolated as a brown solid (11·5 g.; 93%), m. p. 170—174°, which was recrystallised from benzene to give the glycol (10·2 g.; 83%) as needles, m. p. 174° (Zalkind and Aizikovitch, *J. Gen. Chem. Russia*, 1937, **7**, 227, give m. p. 173—174°; Kuhn and Wallenfells, *loc. cit.*, give m. p. 170°).

2 : 7-Diphenylocta-3 : 5-diyne-2 : 7-diol.—The reaction was carried out by the general method by using acetophenone (12 g.) with a reaction period of 24 hours. Isolation of the crude product gave a solid (8·8 g.; 61%), m. p. 193—195°, which was recrystallised from benzene to give the pure glycol (8·6 g.) as needles, m. p. 195° (Strauss, Kollek, and Hauptmann, *loc. cit.*, give m. p. 195° and 142—143° for the two stereoisomeric forms).

1 : 1 : 6 : 6-Tetraphenylhexa-2 : 4-diyne-1 : 6-diol.—The reaction was carried out by the general method by using benzophenone (18·2 g.) in dry ether (50 c.c.) with a reaction period of 24 hours. The crude product was a deep-red, very viscous liquid. After several days a benzene solution deposited brown crystals (10·5 g.), m. p. 138—140°, which after recrystallisation from benzene gave the glycol (10·0 g., 48%) as needles, m. p. 140—141° (Kuhn and Wallenfells, *loc. cit.*, give m. p. 140—141°).

3 : 8-Dimethyl-1 : 10-diphenyldeca-1 : 9-diene-4 : 6-diyne-3 : 8-diol.—The reaction was carried out by the general method by using benzylideneacetone (14·6 g.) in dry ether (50 c.c.) with a reaction period of 24 hours. Isolation of the crude product gave a dark-red syrup which was dissolved in dry benzene (100 c.c.) and extracted with ethylene glycol (3 × 100 c.c.). Dilution of the glycol solution with water and isolation with ether gave a light-brown syrup (9 g.; 52%) which could not be induced to crystallise. No satisfactory analytical data could be obtained (Found: C, 82·0; H, 6·5. $C_{24}H_{22}O_2$ requires C, 84·2; H, 6·5%) but the light absorption of the product (Maximum, 2510—2550 A., ε = 27,000) is in accordance with the expected value (styrene has maximum, 2440 A.; ε = 12,000: Hirshberg, *J. Amer. Chem. Soc.*, 1949, **71**, 3241).

The authors thank Mr. E. S. Morton for microanalyses. One of them (J. B. A.) is indebted to the Department of Scientific and Industrial Research for a Maintenance Grant.

THE UNIVERSITY, MANCHESTER, 13. [*Received, August 31st*, 1950.]

10. *Researches on Acetylenic Compounds. Part XXIX. The Reaction between Nickel Carbonyl and Disubstituted Acetylenes.*

By E. R. H. Jones, T. Y. Shen, and M. C. Whiting.

Treatment of disubstituted acetylenes with nickel carbonyl in aqueous-alcoholic acetic acid gives αβ-disubstituted acrylic acids. The stereochemical configuration of the products and, in the case of unsymmetrical acetylenes, the direction of the addition reaction are discussed.

In various summaries of work in the acetylene field carried out in Germany during the war (see *inter al.* Reppe, *Experientia*, 1949, **5**, 93; "Acetylene Chemistry," translation, Meyer and Co., 1949, p. 156) it is stated that the reaction between nickel carbonyl and acetylene, which gives acrylic acid or its derivatives, can be extended to both mono- and di-substituted acetylenes. The application of this reaction, suitably termed the "Reppe carboxylation reaction," to mono-substituted acetylenes has already been examined in detail (Jones, Shen, and Whiting, *J.*, 1950, 230), and this paper deals with its use with certain types of disubstituted acetylenes.

Treatment of the symmetrical hydrocarbons, dec-5-yne and tolan (I; $R^1 = R^2$ = Bu and Ph, respectively) with nickel carbonyl under the conditions previously found to be most favourable for mono-substituted acetylenes, *i.e.*, in aqueous-ethanolic acetic acid at 65—75°, gave the expected acids (II; $R^1 = R^2$ = Bu and Ph, respectively) in *ca.* 40% yields. In the latter case the product was the "*trans*"-α-phenylcinnamic acid (III), m. p. 173°, which gives *cis*-stilbene

$$\underset{\text{(I.)}}{R^1C{\equiv}CR^2} \qquad \underset{\text{(II.)}}{R^1CH{=}CR^2{\cdot}CO_2H} \qquad \underset{\text{(III.)}}{\begin{matrix}PhCH\\ \|\\ PhC{\cdot}CO_2H\end{matrix}} \longrightarrow \begin{matrix}PhCH\\ \|\\ PhCH\end{matrix}$$

on decarboxylation; it therefore seems that *cis*-addition of the hydrogen and carboxyl groups takes place during the reaction. Confirmation of this view was obtained when but-2-yne-1 : 4-diol diacetate (I; $R^1 = R^2 = AcO{\cdot}CH_2$) was treated with nickel carbonyl. The product, the crystalline acid (IV), obtained in 53% yield, gave on alkaline hydrolysis the crystalline dihydroxy-acid (V). Now the *cis*-γ-hydroxy-αβ-ethylenic acids obtained by semihydrogenation

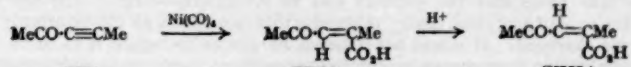
$$\text{(IV.)}\ \begin{matrix}AcO{\cdot}CH_2{\cdot}CH\\ \|\\ AcO{\cdot}CH_2{\cdot}C{\cdot}CO_2H\end{matrix} \longrightarrow \begin{matrix}HO{\cdot}CH_2{\cdot}CH\\ \|\\ HO{\cdot}CH_2{\cdot}C{\cdot}CO_2H\end{matrix}\ \text{(V.)}$$

of the corresponding acetylenes (Haynes and Jones, *J.*, 1946, 954) lactonised very readily. The failure of (V) to cyclise even on being heated to 100° thus proves the *trans*-configuration of the carboxyl and hydroxymethyl substituents, and hence the *cis*-addition of hydrogen and carboxyl to the acetylenic diacetate during the reaction.

Treatment of either hex-1-yne-1-carboxylic acid (I; R^1 = Bu, $R^2 = CO_2H$) or its ethyl ester under the standard conditions resulted in exothermic reactions and the formation, in *ca.* 30% yields, of *n*-butylfumaric acid and of its crystalline monoethyl ester (II; $R^1 = CO_2Et$, R^2 = Bu), respectively. These reactions constitute further clear cases of *cis*-addition. As a synthesis of pure monoesters of monosubstituted fumaric acids, this reaction may be of some synthetic importance, since such esters, with unambiguous structures, are not otherwise easily accessible.

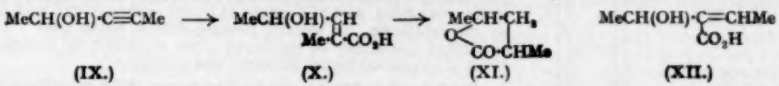
When the ketones, oct-3-yn-2-one and pent-3-yn-2-one (I; R^1 = Bu and Me, respectively; R^2 = Ac) were treated with nickel carbonyl, exothermic reactions occurred and the corresponding acids were obtained in 30—40% yields; the position of the carboxyl group was indicated by their stability, and the direction of the addition is thus analogous to that observed with the acetylenic acid and ester. The product, m. p. 31°, from oct-3-yn-2-one was homogeneous, and analogy with the reactions discussed above suggests that it must be the *trans*-isomer of (II; R^1 = Ac, R^2 = Bu) *i.e.*, that obtained by *cis*-addition to the triple bond. The product from pent-3-yn-2-one (VI), however, was very water-soluble and could be isolated only by continuous ether-extraction of its strongly acidified solution; it proved to be a heterogeneous solid, m. p. 70—75°, from which two isomers, m. p.s 96—97° and 100—101° (VII and VIII), were separated in low yield by fractional crystallisation. The former resembled the acid obtained from oct-3-yn-2-one in its properties and can thus be assigned the *trans*-configuration (VII); the latter, presumably formed by acid-catalysed isomerisation, is the corresponding *cis*-form (VIII) (which actually exists in solution as the tautomeric cyclic pseudo-acid). The properties, chemical and spectrographic, of these keto-acids have been extensively investigated and leave no room for

doubt regarding the assigned configurations; they will be reported, in relation to analogous cases, in a later publication.



(VI.) (VII.) (VIII.)

The failure of secondary and tertiary ethynylcarbinols to react readily with nickel carbonyl has already been mentioned (Jones, Shen, and Whiting, *loc. cit.*). In view of the apparent reluctance of the carboxyl group to enter at a position adjacent to a secondary carbinol grouping, it might be expected that pent-3-yn-2-ol (IX) would give (X), rather than (XII), on treatment with nickel carbonyl. In contrast to the ethynylcarbinols, (IX) reacted readily with nickel carbonyl under the usual conditions, and gave as the acidic reaction product a syrup, b. p. 90° (bath temp.)/10^{-5} mm., which gave analytical data in good agreement with (X) or (XII); the yield, 60%, was unusually high, but the product appeared to be somewhat heterogeneous (striations on distillation, etc.). On hydrogenation with a platinum catalyst (uptake exactly as calculated for one double bond) and distillation, only a 65% yield of αγ-dimethylbutyrolactone (XI)

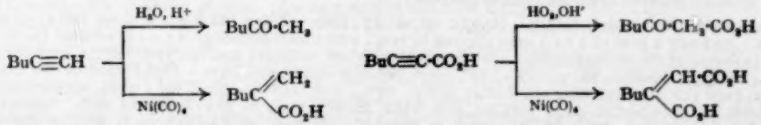


(IX.) (X.) (XI.) (XII.)

was obtained. A less volatile residue remained, which gave a heterogeneous, high-boiling liquid on distillation, either directly or over potassium hydrogen sulphate. It follows that only about 70% of the crude product could have consisted of (X); if (XII) had been present to a significant extent, however, α-ethylcrotonic acid, m. p. 45°, should have been isolated. The nature of the acidic compounds accompanying (X) therefore remains uncertain; etherification of the hydroxyl group in (X) is one possibility.

Certain other experiments on disubstituted acetylenes require brief discussion. But-2-yne-1 : 4-diol reacted exothermically with nickel carbonyl, but no reaction product could be isolated. This is hardly surprising, since (V), prepared from its diacetate, was somewhat unstable (*e.g.*, it could not be reacetylated with acetic anhydride and pyridine). The apparent " success " of the reaction with but-2-yne-1 : 4-diol recalls the similar vigorous reaction observed with propargyl alcohol. The Mannich bases (I; $R^1 = CH_2{\cdot}NEt_2$, R^2 = Bu, and Ph) failed to react exothermically and were to some extent recovered unchanged. The vinylacetylene, 1-*cyclo*hex-1′-enylhex-1-yne, failed to react exothermically and was recovered in 65% yield; the diacetylenes, diphenyldiacetylene, dodeca-5 : 7-diyne, and hexa-2 : 4-diyne, were to some extent decomposed by nickel carbonyl, somewhat exothermally, with the formation of black polymeric material but no appreciable quantity of acidic product; the first two hydrocarbons were recovered in yields of 75 and 60%.

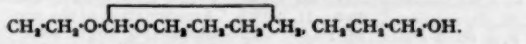
Two conclusions can be drawn concerning the direction of addition in the Reppe carboxylation reaction. The first is that the carbonyl group attacks that carbon atom which in acid-, alkali-, or mercury-salt-catalysed hydration accepts the oxygen atom :



The second is that the reaction only occurs readily when the carbonyl group can attack a triply-bonded carbon atom which is linked to one of a limited number of groups. These are (R = alkyl or aryl) :

Groups facilitating carboxylation (A).

R, $CH_2{\cdot}OH$, $CH_2{\cdot}OAc$ or $CHR{\cdot}OAc$, $CH_2{\cdot}CH_2{\cdot}OH$ or $CH_2{\cdot}CHMe{\cdot}OH$, $CH_2{\cdot}CH_2{\cdot}OAc$



Groups hindering carboxylation (B).

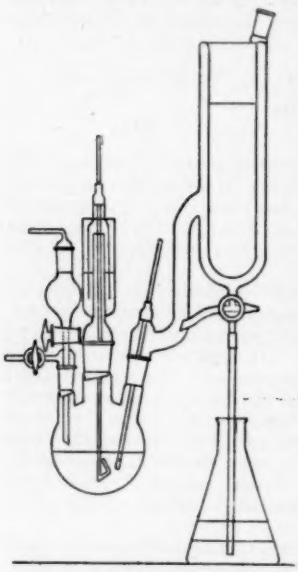
H, $CHR{\cdot}OH$ or $CR_2{\cdot}OH$, $CR_2{\cdot}OAc$, $CH_2{\cdot}CMe_2{\cdot}OH$,
Ac, CO_2H, CO_2Et.

In a compound XC≡CY, if both X and Y are groups of type *A*, rapid reaction occurs; if they are both of type *B*, no rapid reaction occurs; if X is of type *A* and Y is of type *B*, a rapid reaction will take place and the product will be XC(CO_2H)=CHY. The one outstanding exception is the case of acetylene itself; otherwise this rule covers all the vigorously exothermic reactions so far observed. It would nevertheless be unwise to regard it as more than a very tentative generalisation from somewhat limited experience; however, it makes possible certain predictions, *e.g.*, that acetylenedicarboxylic ester would fail to react vigorously. This has been verified; mellitic ester (15% yield) was the only product isolated.

Somewhat similar limitations to the applicability of the Mannich reaction with acetylenic compounds have been observed (Jones, Marszak, and Bader, *J.*, 1947, 1578)

Experimental.

General Method.—The technique used was essentially similar to that previously described (Jones, Shen, and Whiting, *loc. cit.*), except that the apparatus was as now shown. The condenser contains a mixture of carbon tetrachloride and solid carbon dioxide; by turning the three-way tap it could be employed for either reflux or distillation. An atmosphere of nitrogen was maintained throughout the experiment; at the end of the exothermic reaction ether was added, and the excess of nickel carbonyl was removed by co-distillation, an electric heating-mantle being used. This apparatus could also be employed when quantitative determination of unreacted nickel carbonyl was necessary.



Dec-5-ene-5-carboxylic Acid.—Dec-5-yne (13·8 g.) (Hennion, *J. Amer. Chem. Soc.*, 1937, **59**, 1310), ethanol (30 c.c.), water (1·5 c.c.), and glacial acetic acid (4 c.c.) were warmed to 75° and treated with a solution of nickel carbonyl (5 c.c.) in ethanol (5 c.c.). An xothermic reaction occurred; when complete, the excess of carbonyl was removed, and isolation of the acid fraction (by mean of sodium hydroxide solution) gave the *acid* (8·0 g., 44%), b. p. 122°/0·5 mm., n_D^{20} 1·4644 (Found: C, 72·05; H, 10·9. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·95%). On fractionation of the neutral portion of the reaction mixture the corresponding *ethyl* ester (1·6 g., 8%) was obtained; it had b. p. 93°/0·8 mm., n_D^{16} 1·4509 (Found: C, 73·8; H, 11·4. $C_{13}H_{24}O_2$ requires C, 73·5; H, 11·4%). A *by-product* (1·4 g.), b. p. 148°/0·5 mm., n_D^{17} 1·4744, was also isolated (Found: C, 82·1; H, 12·45. $C_{20}H_{34}O$ requires C, 82·1; H, 12·4%). Light absorption: Maximum, 2420 A.; $E_{1\,cm.}^{1\%}$ = 460. It formed a dinitrophenylhydrazone which failed to crystallise even after chromatographic purification; its constitution was not investigated further.

Dec-5-ene-5-carboxylic acid gave an S-*benzylthiuronium* salt, which formed needles, m. p. 129°, from aqueous methanol (Found: C, 65·6; H, 8·45. $C_{18}H_{30}O_2N_2S$ requires C, 65·1; H, 8·65%), and a p-*phenylphenacyl* ester which formed plates, m. p. 42°, from aqueous methanol (Found: C, 79·2; H, 7·8. $C_{33}H_{36}O_3$ requires C, 79·3; H, 8·0%). Its *p*-nitrobenzyl ester formed needles, m. p. 29°, from methanol. Esterification of the acid with ethanol and sulphuric acid gave an ester, b. p. 70°/0·05 mm., n_D^{17} 1·4508 agreeing well with the constants of the material isolated from the neutral fraction.

trans-α-*Phenylcinnamic Acid* (cf. Reppe, *op. cit.*, p. 156).—Tolan (13·5 g.), ethanol (40 c.c.), water (1·5 c.c.), and acetic acid (3·5 c.c.) were allowed to react with nickel carbonyl (4 c.c.) in ethanol (10 c.c.) at 70°. Isolation of the acidic fraction, after removal of excess carbonyl, and recrystallisation gave the acid (6·3 g., 38%) as needles, m. p. 172—173°, from benzene–light petroleum. Distillation of the neutral fraction gave the corresponding ethyl ester (2·0 g., 10%), b. p. 142°/0·8 mm., n_D^{17} 1·5986, which solidified on storage and then had m. p. 31° (Müller, *Ber.*, 1893, **26**, 659, gives m. p. 172° for the acid; Auwers and Eisenlohr, *J. pr. Chem.*, 1911, **84**, 87, give b. p. 214—215°/28 mm., $n_D^{18\cdot6}$ 1·5972, m. p. 28°, for the ethyl ester). Hydrolysis of the ethyl ester (0·5 g.) with aqueous-methanolic sodium hydroxide solution at 20° for 18 hours, followed by isolation of the acid fraction and recrystallisation gave the acid (0·2 g.), m. p. 173° undepressed on admixture with the specimen obtained directly from the reaction.

1 : 4-*Diacetoxybut-2-ene-2-carboxylic Acid* (IV).—A solution of but-2-yne-1 : 4-diol diacetate (19 g.) (Valette, *Ann. Chim.*, 1948, **3**, 644), ethanol (40 c.c.), water (2·5 c.c.), and acetic acid (4·5 c.c.) was treated with a solution of nickel carbonyl (6 c.c.) in ethanol (10 c.c.) at 65°. Isolation of the acid fraction gave a solid which was crystallised from benzene to give the *diacetoxy-acid* (12·5 g., 53%), as needles, m. p. 65° (Found: C, 49·9; H, 5·6. $C_9H_{12}O_6$ requires C, 50·0; H, 5·6%). Fractionation of the neutral portion gave (*a*) a liquid (1·2 g., 5%), b. p. 60°/0·1 mm., n_D^{17} 1·4450, which appeared to be the somewhat impure *ethyl* ester corresponding to the diacetoxy-acid (Found: C, 56·4; H, 6·95; OEt, 18·3. $C_8H_{11}O_4{\cdot}CO_2Et$ requires C, 54·1; H, 6·45; OEt, 18·4%); and (*b*) a *substance*, b. p. 150° (bath temp.)/10^{-4} mm., n_D^{16} 1·4710, which solidified when kept and was recrystallised from methanol to give prisms, m. p. 98° (0·4 g.) [Found: C, 56·1; H, 6·35%; *M* (ebullioscopic), 276. $C_{12}H_{16}O_6$ requires C, 56·3; H, 6·25%; *M*, 256].

Its saponification value corresponded to the presence of 3·2 ester groupings per molecule; it showed a light-absorption maximum at 2300 A., $\varepsilon = 10{,}000$. No structure can be suggested for this substance.

1 : 4-*Dihydroxybut-2-ene-2-carboxylic Acid* (V).—The corresponding diacetoxy-acid (9·9 g.) was treated with a solution of potassium hydroxide (10 g.) in water (20 c.c.) and ethanol (60 c.c.). After 16 hours at 20° the solution was diluted, strongly acidified, and extracted continuously with ether for two days. Evaporation of the ether gave a dark syrup which slowly crystallised on being kept at 0°; recrystallisation from benzene–dioxan yielded the *dihydroxy-acid* (0·9 g.) as prisms, m. p. 89—90° (Found: C, 45·4; H, 6·25. $C_4H_6O_4$ requires C, 45·5; H, 6·1%). No moderately-volatile material (b. p. >20°/0·2 mm.) was obtained on distillation of the hygroscopic syrup obtained by evaporating the mother-liquors.

4-*Hydroxypent-2-ene-2-carboxylic Acid* (X).—A solution of pent-3-yn-2-ol (IX) (16·8 g.) (Iositch *et al.*, *J. Russ. Phys. Chem. Soc.*, 1909, **41**, 529; *Bull. Soc. chim.*, 1910, **8**, 889) in ethanol (50 c.c.), water (4 c.c.), and acetic acid (8 c.c.) was treated with a solution of nickel carbonyl (8 c.c.) in ethanol (15 c.c.) at 75° in the usual way, an exothermic reaction taking place. After removal of excess of carbonyl, the acidic fraction was isolated by continuous ether extraction, washing with potassium hydrogen carbonate solution and continuous re-extraction after acidification. The dried extract was concentrated by evaporation and distilled at 85—90° (bath temp.)/10^{-3} mm., to give a viscous oil (15·1 g., 60%), n_D^{15} 1·4908 (Found: C, 55·5; H, 7·9. Calc. for $C_6H_{10}O_3$: C, 55·35; H, 7·8%). As the oil could not be induced to crystallise it was impossible to estimate the proportion of the 4-hydroxypent-2-ene-2-carboxylic acid present; from the analytical data it cannct have contained much non-isomeric material, and the hydrogenation data given below show that the proportion of the expected acid cannot have been less than 65%. It readily gave a crystalline p-*nitrobenzyl* ester (prisms, m. p. 98°, from benzene–light petroleum), which is assumed to be that of the principal component (Found: C, 58·6; H, 5·65. $C_{13}H_{15}O_5N$ requires C, 58·85; H, 5·7%). *Hydrogenation*: the oily acid (6·0 g.) was dissolved in methyl acetate and shaken in hydrogen in the presence of platinic oxide (25 mg.); absorption ceased after the uptake of 99% of the volume calculated for the reduction of one double bond. The removal of catalyst, evaporation of the solvent, and distillation of the residue gave αγ-dimethylbutyrolactone (XI) (3·4 g., 65%), b. p. 50°/0·1 mm., 110°/18 mm., n_D^{15} 1·4296 (Found: C, 62·7; H, 8·6. Calc. for $C_6H_{10}O_2$: C, 63·1; H, 8·85%). Treatment with hydrazine hydrate gave the hydrazide of γ-hydroxy-α-methylvaleric acid as needles, m. p. 117—118°, from ethyl acetate. (Boorman and Linstead, *J.*, 1935, 267, give b. p. 81°/10 mm., n 1·4289, for the lactone and m. p. 118° for the hydrazide.) The residue from the distillation of the lactone (1·6 g.) was distilled at 140—190° (bath temp.)/10·5 mm. over potassium hydrogen sulphate to give a heterogeneous liquid (1·0 g.); no crystalline material could be isolated.

n-*Butylfumaric Acid*.—Hex-1-yne-1-carboxylic acid (9·5 g.) (Haynes and Jones, *J.*, 1946, 503), ethanol (30 c.c.), acetic acid (4 c.c.), and water (2 c.c.) were treated with nickel carbonyl (5 c.c.) in ethanol at 75° by the general method. Isolation of the acidic fraction gave, after recrystallisation from benzene–ethanol, n-butylfumaric acid (3·6 g., 28%), m. p. 169—170° (Fittig and Fichter, *Annalen*, 1899, **304**, 250, give m. p. 170°). A small amount of a liquid, b. p. 130°/0·2 mm., n_D^{21} 1·4660, was obtained on distilling the non-crystalline portion of the acid fraction; it probably consisted of a mixture of impure monoethyl esters.

α-n-*Butyl-β-carbethoxyacrylic Acid*.—Ethyl hex-1-yne-1-carboxylate (6·0 g.) (Haynes and Jones, *loc. cit.*) in ethanol (25 c.c.), acetic acid (4 c.c.), and water (1·5 c.c.) was treated with a solution of nickel carbonyl (3 c.c.) at 65°. An exothermic reaction occurred, and isolation of the acidic product gave the *half-ester* (2·0 g., 25%), as a liquid, b. p. 120°/0·1 mm., which solidified on storage and was recrystallised from light petroleum (b. p. 40—60°) to give needles, m. p. 45° (Found: C, 60·1; H, 7·6. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·05%). *Hydrolysis*. Treatment of the half-ester with excess of potassium hydroxide solution at 20° gave on isolation the dicarboxylic acid, m. p. 167° undepressed on admixture with a specimen obtained as above.

2-*Keto-oct-3-ene-4-carboxylic Acid*.—A solution of oct-3-yn-2-one (9·3 g.) (Nieuwland, *J. Amer. Chem. Soc.*, 1936, **58**, 1862) in ethanol (25 c.c.), water (2 c.c.), and acetic acid (6 c.c.) was treated with nickel carbonyl (5 c.c.) at 65°, and a smooth exothermic reaction took place. Distillation of the acidic portion of the reaction product furnished the *keto*-acid (5·1 g., 40%) as a liquid, b. p. 115°/0·1 mm., n_D^{18} 1·4713, which crystallised on storage. On recrystallisation from light petroleum (b. p. 60—80°) at −40° it formed plates, m. p. 30—31° (Found: C, 63·55; H, 8·1. $C_9H_{14}O_3$ requires C, 63·55; H, 8·2%).

4-*Ketopent-2-ene-2-carboxylic Acid*.—To a solution of pent-3-yn-2-one (7·0 g.) (Braude, Jones, Sondheimer, and Toogood, *J.*, 1949, 609) in methanol (35 c.c.), water (2 c.c.), and acetic acid (4 c.c.), nickel carbonyl (5 c.c.) was added at 65°; an exothermic reaction took place, a brown coloration becoming evident whenever the rate of addition was increased. After removal of excess of carbonyl, isolation of the acidic fraction by ether extraction gave a heterogeneous solid (3·15 g., 30%), m. p. 70—75°. Recrystallisation from water gave, in small yield, the *trans*-acid as plates, m. p. 96—97° unchanged on further recrystallisation (Found: C, 56·25; H, 6·55. Calc. for $C_5H_6O_3$: C, 56·25; H, 6·25%. Two recrystallisations of the acid, m. p. 70—75°, from benzene gave the *cis*-acid as needles, m. p. 100—101° unchanged on further recrystallisation (Found: C, 56·5; H, 6·4%). A mixture of the two forms melted at 68—78°. The evidence upon which the assigned configurations have been based will be given in a forthcoming publication [Ajjello and Cusmano, *Gazzetta*, 1940, **70**, 512, give m. p. 98° for an acid of this constitution but unknown configuration; Baxter, Norris, and Morris, *J.*, 1949, 95, give m. p. 102—102·5° (" needles from benzene ") for what was in all probability the *cis*-form].

From the neutral fraction a *methyl* ester (350 mg.), b. p. 44—46°/0·2 mm., was isolated by distillation. It solidified completely on being kept, and was recrystallised from light petroleum (b. p. 40—60°) at −40° to give prisms, m. p. 41° (Found: C, 58·85; H, 7·15. $C_7H_{10}O_3$ requires C, 59·1; H, 7·1%).

Ethyl Mellitate.—Ethyl acetylenedicarboxylate (3·6 g.) in ethanol (25 c.c.) water (0·5 c.c.), and acetic acid (11·5 c.c.) was treated slowly with nickel carbonyl (1·5 c.c.) in ethanol (5 c.c.) at 65—70°

for 10 minutes. No exothermic reaction occurred; removal of excess of carbonyl and isolation of the neutral fraction gave a blue semi-solid mass, which was filtered off. On recrystallisation, the solid portion gave ethyl mellitate (0·65 g., 18%), m. p. 74° (Found: C, 56·25; H, 6·2. Calc. for $C_{24}H_{30}O_{12}$: C, 56·45; H, 5·9%) (Kraut and Busse, *Annalen*, 1875, **177**, 273, give m. p. 72·5—73°). Distillation of the mother-liquors gave unchanged ethyl acetylenedicarboxylate (0·63 g., 17%), b. p. 48—50°/0·2 mm., n_D^{20} 1·4410, m. p. 1°; no other substance could be isolated from the neutral fraction, nor was any appreciable quantity of acidic product formed.

The nickel carbonyl used in this investigation was kindly provided by the Mond Nickel Co. The authors thank Mr. E. S. Morton for microanalyses. One of them (T. Y. S.) is indebted to the Universities' China Committee for a maintenance grant.

THE UNIVERSITY, MANCHESTER, 13. [*Received, August 31st*, 1950.]

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11. *Aminoalkyl Tertiary Carbinols and Derived Products. Part IV. Spasmolytics. Phenyl- and cyclo*Hexylphenyl-carbinols.

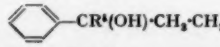
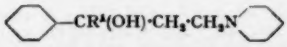
By D. W. ADAMSON, P. A. BARRETT, and S. WILKINSON.

A number of 3-amino-1-phenylalkan-1-ols (I; R^1 = alkyl) and 1-*cyclo*hexyl-3-piperidinoalkan-1-ols (II; R^1 = alkyl) were prepared by conventional methods for pharmacological testing.

Amino-1-*cyclo*hexyl-1-phenylalkan-1-ols (III and VII), of interest as spasmolytics, were obtained by controlled partial hydrogenation of the corresponding amino-1 : 1-diphenylalkan-1-ols (IV and VI); complete hydrogenation gave the di*cyclo*hexyl compounds.

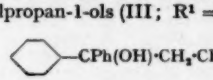
Compounds derived from the amino-carbinols by dehydration and subsequent reduction are described.

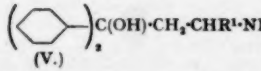
A NUMBER of phenylalkanolamines (I; R^1 = alkyl) and *cyclo*hexylphenylalkanolamines (I; $R^1 = CH{<}C_5H_{10}$) were prepared several years ago for pharmacological testing, as part of our programme in this series (Parts I—III; *J.*, 1949, S144; 1950, 885, 1039); the former are the subject of B.P. Appln. 5932/48. A number of these compounds were described recently by Denton, Lawson, Neier, Schedl, and Turner (*J. Amer. Chem. Soc.*, 1949, **71**, 2050, 2053, 2054) and by Ruddy and Buckley (*ibid.*, 1950, **72**, 718). The compounds are of interest as spasmolytics (White and Green, personal communication; Becker, Ananenko, Glenwood, and Miller, *Fed. Proc.*, 1946, **5**, 163; Cunningham *et al.*, *J. Pharm. Exp. Ther.*, 1949, **96**, 151) and it has been reported that 1-*cyclo*hexyl-1-phenyl-3-piperidinopropan-1-ol (I; $R^1 = CH{<}C_5H_{10}$, $NR^2R^3 = N{<}C_5H_{10}$) is a valuable drug in the treatment of Parkinsonism (Doshay and Constable, *J. Amer. Med. Assoc.*, 1949, **140**, 1317; Ellenbogen, *Lancet*, 1950, **1**, 1034; Phillips, Montuschi, and Shakey, *ibid.*, p. 1131).

(I.)  (II.) 

3-Amino-1-phenylalkan-1-ols (I; R^1 = alkyl) were prepared by the same method as that described in the above-mentioned papers, namely, reaction between an alkylmagnesium bromide and the appropriate β-aminopropiophenone. The compounds of this series which have not already been described are included in Table I. The *O*-acetyl and *O*-benzoyl derivatives of the carbinols (I; R^1 = Me, $NR^2R^3 = NMe_2$ and $N{<}C_5H_{10}$) were also prepared. The phenylalkanol amines (I; R^1 = alkyl, $NR^2R^3 = N{<}C_5H_{10}$) were hydrogenated in the presence of platinum to the corresponding 1-*cyclo*hexyl-3-piperidinoalkan-1-ols (II; R^1 = alkyl).

The Grignard reaction was used also in the first instance for the synthesis of 3-amino-1-*cyclo*hexyl-1-phenylpropan-1-ols (III; R^1 = H), but, as found by other workers, the yields were poor

(III.)  $CPh_2(OH)\cdot CH_2\cdot CHR^1\cdot NR^2R^3$ (IV.)


(V.)

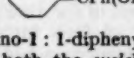
(*ca.* 10%). The product from the reaction between *cyclo*pentylmagnesium bromide and β-piperidinopropiophenone was a mixture of bases, from which only 1-phenyl-3-piperidino-

propan-1-ol (I; $R^1 = H$, $NR^2R^3 = N{<}C_5H_{10}$), arising by reduction of the amino-ketone, could be isolated. The propensity of *cyclo*pentylmagnesium bromide to reduce instead of add to ketones was discussed by Kharasch and Weinhouse (*J. Org. Chem.*, 1936, **1**, 209), and recently Hey and Musgrave (*J.*, 1949, 3156) noted that reduction of the carbonyl groups occurred in place of normal addition in the reaction between this Grignard reagent and deoxybenzoins.

A more satisfactory route to the *cyclo*hexylphenylcarbinols (III; R^1 = H or alkyl) was found in the catalytic hydrogenation of the readily available 3-amino-1 : 1-diphenylalkan-1-ols (IV; R^1 = H or alkyl) (Part I, *loc. cit.*, and Part V, to follow). In the presence of Adams's platinum catalyst, the diphenylcarbinols absorbed hydrogen as a continuous process, finally to give the di*cyclo*hexylcarbinols (V), there being no abrupt change in the rate of absorption at a point which would correspond to the saturation of only one of the phenyl groups. However, the hydrogenation followed, to a large degree, a stepwise course for it was possible to stop the reduction at a stage which allowed of the isolation in good yield, of the desired *cyclo*hexylphenylcarbinols (III). This is substantially in accord with the conclusions, based on the kinetic and analytical study of the catalytic hydrogenation of compounds containing more than one phenyl nucleus, recorded by Smith, Aldermann, Shacklett, and Welch (*J. Amer. Chem. Soc.*, 1949, **71**, 3772).

The process was examined in detail for the *cyclo*hexylphenylcarbinols which were of particular pharmacological interest. It was expedient to allow absorption of 10—15% in excess of the 3 moles of hydrogen theoretically required, otherwise unchanged diphenylcarbinol, difficult to remove by crystallisation, was present in the product. On the other hand, the fully saturated di*cyclo*hexylcarbinols were readily removed by crystallisation of the basic product, by virtue of their high solubility in organic solvents. The purified products were identical with those prepared from *cyclo*hexylmagnesium bromide and the appropriate β-aminopropiophenone. The ultra-violet absorption spectra, for measurements of which we are indebted to Dr. T. S. G. Jones, as well as mixed melting points with authentic specimens, provided evidence for the structure and purity of the products. As purification proceeded, the fine structure of the absorption band associated with the presence of one phenyl group became more sharply defined and finally was identical with that of the authentic specimens (light absorption in ethanolic solution : maximum, λ 258·5 mμ.; ε 233—250). In other cases, when the basic product did not crystallise and where there was no unequivocal specimen available for comparison, purification was effected by recrystallisation of a salt (hydrochloride or hydrogen oxalate), constancy of m. p. and definition of the ultra-violet spectrum being taken as criteria of purity.

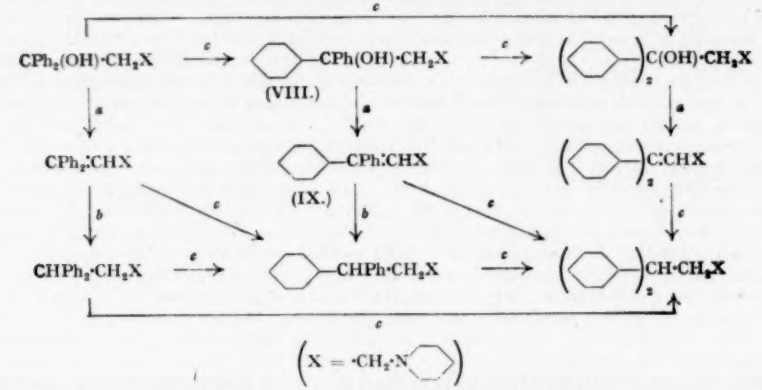
Hydrogenation of diphenylcarbinols substituted in the chain in the 3-position (IV; R^1 = Me or Pr^n; to be described in Part V) proceeded more slowly than that of those lacking the substituent. An example in which the substituent was in the 2-position, *viz.*, 2-methyl-1 : 1-diphenyl-3-piperidinopropan-1-ol, was resistant to hydrogenation under the conditions of our experiments. Hydrogenation was considerably slower when the phenyl groups were substituted as in 3-piperidino-1 : 1-di-*p*-tolylpropan-1-ol, absorption ceasing when only one of the *p*-tolyl groups was saturated.

(VI.) $CPh_2(OH)\cdot[CH_2]_n\cdot NR^1R^2$  $CPh(OH)\cdot[CH_2]_n\cdot NR^1R^2$ (VII.)

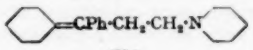
The process was also applied to some ω-amino-1 : 1-diphenylalkan-1-ols (VI; n = 4, 5, 6; to be described in a later paper) from which both the *cyclo*hexylphenyl- and di*cyclo*hexylcarbinols could be prepared. An alternative route was followed in one example : in the catalytic hydrogenation of 5-bromo-1 : 1-diphenylpentan-1-ol, saturation of the first phenyl group was rapidly completed but further reduction was very slow, thereby facilitating the isolation of 5-bromo-1-*cyclo*hexyl-1-phenylpentan-1-ol, from which the 5-piperidino-compound (VII; n = 4, $NR^1R^2 = N{<}C_5H_{10}$) was prepared.

It was of interest to prepare the corresponding alkenyl- and alkyl-amines from the carbinols by dehydration and subsequent reduction, especially since earlier work in these laboratories had shown that some related dithienylalkenylamines were potent analgesics (Part II, *loc. cit.*, Adamson and Green, *Nature*, 1950, **165**, 122) and that phenylpyridylalkenylamines had a powerful antihistamine action (Part III, *loc. cit.*). A series of products of potential pharmacological interest was obviously available from the diphenylcarbinols by adopting combinations of the following processes : (*a*) dehydration, (*b*) hydrogenation of ethylenic linkage in the presence of palladium, (*c*) hydrogenation of ethylenic linkage if present and of one or both phenyl groups in the presence of platinum. This series of reactions was applied to 1 : 1-diphenyl-3-piperidinopropan-1-ol as shown in the appended scheme, and in part to other carbinols as recorded in the experimental section.

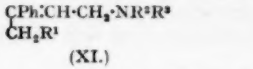
It was possible that dehydration of 1-*cyclo*hexyl-1-phenyl-3-piperidinopropan-1-ol (VIII) had given either 1-*cyclo*hexyl-1-phenyl-3-piperidinoprop-1-ene (IX) or the isomeric 1-*cyclo*hexylidene-1-phenyl-3-piperidinopropane (X), both structures being compatible with the ultra-violet absorption spectrum which exhibited a peak corresponding to the presence of the Ph·C:C group in the molecule. The structure (IX) is assigned to the compound on the basis of its oxidation by potassium permanganate to *cyclo*hexyl phenyl ketone. Two other unsaturated amines isomeric with (IX), *viz.*, 1-*cyclo*hex-1′-enyl- and 1-*cyclo*hex-2′-enyl-1-phenyl-3-piperidinopropane, have been described by Jackman, Nachod, and Archer (*J. Amer. Chem. Soc.*, 1950, **72**, 716) and another, of undetermined structure, by Ruddy and Buckley (*loc. cit.*).



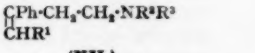
The 3-amino-1-phenylalkan-1-ols (I; R^1 = alkyl) were dehydrated, and some of the alkenylamines so formed catalytically hydrogenated to 1-amino-3-phenylalkanes. The alkenylamine derived from 3-phenyl-1-piperidinononan-3-ol (I; $R^1 = C_6H_{13}$, $NR^2R^3 = N{<}C_5H_{10}$) gave *n*-hexyl phenyl ketone on oxidation and was therefore (XI; $R^1 = C_5H_{11}$, $NR^2R^3 = N{<}C_5H_{10}$). It is assumed that the other alkenylamines also had the allylamine structure (XI), although it is possible that the isomers (XII) were present in minor quantity since the salts of the bases melted over a range and several crystallisations were necessary to attain purity.



(X.)



(XI.)



(XII.)

The compounds now described have been examined for pharmacological properties by Dr. A. C. White and Mr. A. F. Green, of the Biological Division of these Laboratories; they were chiefly of interest on account of their high spasmolytic activity, and a new compound, 1-*cyclo*hexyl-1-phenyl-3-pyrrolidinopropan-1-ol (III; R^1 = H, $NR^2R^3 = N{<}C_4H_8$), and the known piperidino-analogue (VIII) were outstanding in this respect. Some compounds, particularly the quaternary salts derived from the carbinols, had a very strong mydriatic effect, and others were powerful local anæsthetics. Antihistamine activity was not pronounced and no analgesic action was observed. The results of pharmacological examination will be reported elsewhere.

Experimental.

3-Amino-1-phenylalkan-1-ols (Table I, Nos. 1—8).—The *β-tert.*-aminopropiophenone hydrochloride (0·2 mol.) was added in small portions to an ethereal solution of the Grignard reagent made from the appropriate bromoalkane (0·6 mol.). The mixture was then boiled under reflux for 3½ hours in a water-bath kept at 55—65°. The resulting pasty mass was decomposed with crushed ice (100 g.) and 25% aqueous ammonium chloride (150 c.c.), acidified with glacial acetic acid at 0°, and kept in the refrigerator overnight. The bulky precipitate of crude amino-carbinol hydrobromide was filtered off and washed with ether. It was suspended in chloroform and basified by addition of excess of aqueous ammonia, with mechanical stirring. The mixture was filtered, and the chloroform layer separated, washed with water, and dried (Na_2SO_4), and the solvent removed by distillation. The residual crude *amino-carbinols*, when solid, were usually recrystallised from light petroleum (b. p. 40—60°) at low temperatures (acetone–carbon dioxide bath); the yields of purified product were of the order of 60—70%. Those which did not solidify on cooling were purified by distillation under reduced pressure; the yields in these instances were

TABLE I.

3-Amino-1-phenyl- and 3-Amino-1-cyclohexyl-alkan-1-ols, $CR^1R^2(OH)\cdot CH_2\cdot CH_2\cdot NR^3R^4$.

No.	R^1.	R^2.	NR^3R^4.	Formula.	M. p. or b. p.	Solvent for recrystn.*	Analyses. Found, %. C.	H.	N.	Cl.	Required, %. C.	H.	N.	Cl.
1	Ph	CH_3	NMe_2	$C_{12}H_{19}ON$	54°/0·05 mm.	—	75·0	9·8	6·9	—	74·6	9·8	7·3	—
				$C_{12}H_{19}ON,HCl$	165—166°	EtOH–$COMe_2$	—	—	—	15·5	—	—	—	15·5
2	Ph	$C_4H_9^n$	NMe_2	$C_{16}H_{25}ON$	45—46	Petrol	76·7	10·7	6·2	—	76·6	10·6	6·0	—
				$C_{16}H_{25}ON,HCl$	151—152	EtOH–EtOAc	—	—	—	13·2	—	—	—	13·1
3	Ph	$C_3H_7^n$	NEt_2	$C_{16}H_{27}ON$	106—108/0·1 mm.	—	—	—	—	—	—	—	—	—
				$C_{16}H_{27}ON,HCl$	158—160	$CHCl_3$–EtOAc	66·9	9·8	4·8	12·8	67·3	9·5	4·9	12·4
4	Ph	$C_5H_{11}^n$	NEt_2	$C_{18}H_{31}ON$	130—136/0·1 mm.	—	—	—	—	—	—	—	—	—
				$C_{18}H_{31}ON,HCl$	206—208	$CHCl_3$–EtOAc	69·1	9·6	4·5	11·5	68·9	10·2	4·5	11·3
5	Ph	$PhCH_2$	NEt_2	$C_{20}H_{27}ON$	54—55	Petrol	81·0	8·9	4·7	—	80·8	9·1	4·7	—
				$C_{20}H_{27}ON,HCl$	186—187	EtOH	—	—	—	10·6	—	—	—	10·6
6	Ph	$C_3H_7^n$	NBu_2^n	$C_{20}H_{35}ON$	136—138/0·1 mm.	—	—	—	—	—	—	—	—	—
				$C_{20}H_{35}ON,HCl$	115—117	$COMe_2$	69·8	10·4	4·0	10·5	70·3	10·5	4·1	10·4
7	Ph	$C_6H_{12}^n$	$N<C_5H_8^s$	$C_{20}H_{31}ON$	75—75·5	EtOH	79·3	10·2	5·0	—	79·7	10·3	4·7	—
				$C_{20}H_{31}ON,HCl$	190—191	EtOH	—	—	—	10·7	—	—	—	10·5
8	Ph	$C_6H_{17}^n$	$N<C_6H_9O$	$C_{21}H_{33}O_2N$	52—54	Petrol	75·5	10·6	4·1	—	75·7	10·5	4·2	—
				$C_{21}H_{33}O_2N,HCl$	195—197	$CHCl_3$–EtOAc	—	—	—	9·9	—	—	—	9·6
9	$CH<C_5H_{10}$	C_2H_5	$N<C_5H_{10}$	$C_{14}H_{25}ON,HCl$	176—177	EtOH–Et_2O	66·2	11·0	5·0	11·9	66·3	11·1	4·8	12·3
10	$CH<C_5H_{10}$	$C_2H_7^i$	$N<C_5H_{10}$	$C_{17}H_{32}ON,HCl$	150—152	EtOH–Et_2O	67·1	11·3	4·6	—	67·2	11·2	4·6	—
11	$CH<C_5H_{10}$	$C_5H_{11}^n$	$N<C_5H_{10}$	$C_{18}H_{37}ON,HCl$	200	EtOH–Et_2O	69·0	11·1	4·1	10·9	68·8	11·5	4·2	10·7
12	$CH<C_5H_{10}$	$C_6H_{13}^n$	$N<C_5H_{10}$	$C_{20}H_{39}ON,HCl$	192—194	EtOH–Et_2O	69·6	11·5	4·2	—	69·5	11·6	4·1	—

* $N<C_5H_8^s$ = 1 : 2 : 5 : 6-Tetrahydropyridino-.

* Petrol = light petroleum (b. p. 40—60°).

somewhat lower. The *hydrochlorides* of the amino-carbinols were prepared by passing dry hydrogen chloride into a solution of the base in chloroform until acidity to Congo-red was reached. Ether was then added cautiously, with scratching, to the point of crystallisation.

The *β-tert.*-aminopropiophenone hydrochlorides required as starting materials were prepared by the Mannich reaction (Blicke, "Organic Reactions," 1942, vol. 1, p. 303; Part III, *loc. cit.*). *β-(1 : 2 : 5 : 6-Tetrahydropyridino)propiophenone hydrochloride* had m. p. 187—188° after recrystallisation from ethanol (Found: Cl, 14·1. $C_{14}H_{17}ON,HCl$ requires Cl, 14·1%). *β-Di-n-butylaminopropiophenone hydrochloride* had m. p. 61° after recrystallisation from ethyl acetate–ether (Found: N, 4·8; Cl, 12·1. $C_{17}H_{27}ON,HCl$ requires N, 4·7; Cl, 11·9%).

Amino-carbinol Esters.—The amino-carbinol was dissolved in a small volume of anhydrous acetone, cooled to 0°, and a small excess of the acid chloride added dropwise with stirring. The solution was kept for several hours, and the product which separated was filtered off, washed with acetone, and recrystallised from chloroform–acetone. The following were prepared: *3-acetoxy-1-dimethylamino-3-phenylbutane hydrochloride*, m. p. 175° (Found: C, 13·3. $C_{14}H_{21}O_2N,HCl$ requires Cl, 13·1%); *3-benzoyloxy-1-dimethylamino-3-phenylbutane hydrochloride*, m. p. 178—180° (Found: Cl, 10·9. $C_{19}H_{23}O_2N,HCl$ requires Cl, 10·7%); *3-acetoxy-3-phenyl-1-piperidinobutane hydrochloride*, m. p. 168—170° (Found: Cl, 11·8. $C_{17}H_{25}O_2N,HCl$ requires Cl, 11·4%); *3-benzoyloxy-3-phenyl-1-piperidinobutane hydrochloride*, m. p. 175—177° (Found: Cl, 9·9. $C_{22}H_{27}O_2N,HCl$ requires C, 9·5%).

1-cyclo*Hexyl*-*3-piperidinoalkan*-1-*ols* (Table I, Nos. 9—12).—The 1-phenyl-3-piperidinoalkan-1-ol (3·0 g.; prepared in a similar manner to that described by Denton *et al.*, *loc. cit.*) was dissolved in glacial acetic acid (30 ml.) to which Adams's platinum catalyst (1·0 g.) was added, and the mixture shaken in an atmosphere of hydrogen. When absorption was complete, the catalyst was filtered off, and the filtrate diluted with water and basified in the cold with potassium hydroxide. The liberated base was extracted with ether, and the ethereal solution washed with water, dried (Na_2SO_4), and evaporated. The oily products were converted into the *hydrochlorides*, which were recrystallised.

3-Amino-1-cyclo*hexyl*-1-*phenylpropan*-1-*ols by the Grignard Reaction* (Table II, Nos. 2, 3, 5, 8, 11).—The amino-carbinols were prepared from the appropriate β-aminopropiophenone hydrochloride and *cyclo*hexylmagnesium bromide under conditions essentially the same as those described above. The yields of purified product were 10—12%.

The product from the reaction between *cyclo*pentylmagnesium bromide and β-piperidinopropiophenone hydrochloride was an oil which on distillation gave a fraction of b. p. 120—123°/0·1 mm. (42% yield) and a considerable quantity of non-volatile material. The volatile fraction solidified on storage (m. p. 43—45°) and after three crystallisations from ethyl acetate had m. p. 59—61° (Found: C, 76·6; H, 9·3; N, 6·8. Calc. for $C_{14}H_{21}ON$: C, 76·7; H, 9·6; N, 6·4%). The base was converted into the hydrochloride which, after recrystallisation from ethanol–ethyl acetate, had m. p. 136—138° not depressed on admixture with a specimen of 1-phenyl-3-piperidinopropan-1-ol hydrochloride, prepared by catalytic reduction of β-piperidinopropiophenone hydrochloride (Found: N, 5·5; Cl, 13·9. Calc. for $C_{14}H_{21}ON,HCl$: N, 5·5; Cl, 13·9%). Mannich and Lammering (*Ber.*, 1922, **55**, 3510) describe the base as having m. p. 68—69°, hydrochloride, m. p. 138°.

Quaternary Iodides (Table II, Nos. 4, 6, 7, 9, 10, 12).—The methiodides were prepared by mixing the amino-carbinol in a small volume of acetone with an excess (*ca.* 2 mols.) of methyl iodide. After several hours the product was filtered off and recrystallised. The ethiodides were prepared by adding an excess of ethyl iodide to a solution of the amino-carbinol in ethanol and boiling under reflux for 3 hours.

Amino-1-cyclo*hexyl*-1-*phenylalkan*-1-*ols by Catalytic Reduction.*—1-cyclo*Hexyl*-1-*phenyl*-3-*pyrrolidinopropan*-1-*ol* (Table II, No. 5). 1 : 1-Diphenyl-3-pyrrolidinopropan-1-ol (3 g.) (Part I, *loc. cit.*) was dissolved in glacial acetic acid (15 ml.), Adams's platinum catalyst (2·5 g.) (*Org. Synth.*, 1932, Coll. Vol. I, p. 452) added, and the mixture shaken in an atmosphere of hydrogen until the equivalent of 3·4 mols. had been taken up (2 hours). Water was added, the catalyst removed by filtration, excess of ammonia added, and the liberated base extracted with ether. The ethereal solution was dried ($MgSO_4$) and evaporated. The residue (2·9 g.) had m. p. 69—75°. Crystallisation from light petroleum (b. p. 40—60°) (4 ml.) gave 1·9 g., m. p. 82—84°; recrystallisation gave 1-*cyclo*hexyl-1-phenyl-3-pyrrolidinopropan-1-ol (1·8 g.; 60%), m. p. 85·5—86·5°, not depressed on admixture with the compound prepared by the Grignard reaction, and giving an identical absorption spectrum (light absorption in 0·17% solution in ethanol: maximum, λ 258·5 mμ., ε 233). The light absorption of a 0·17% ethanolic solution of the corresponding diphenylcarbinol was maximal at λ 258·5 mμ., ε 520.

The experiment was repeated, reductions being stopped when different amounts of hydrogen had been absorbed, and the products recrystallised until pure (m. p. and absorption spectrum). The yields obtained when 3·5 and 4·0 mols. of hydrogen were absorbed were 42 and 23%, respectively; a pure product was not obtained from hydrogenations in which 3·25 mols. or less were absorbed. In an experiment on a larger scale, in which the diphenylcarbinol (30 g.), glacial acetic acid (120 ml.), and platinum catalyst (6 g.) were employed, the hydrogen absorption was stopped at 3·4 mols. after 9 hours; the yield of product (m. p. 84—86°) after three crystallisations was 19·3 g. (64%).

1-cyclo*Hexyl*-1-*phenyl*-3-*piperidinopropan*-1-*ol* (Table II, No. 8). Several small-scale hydrogenations, similar to those described above were carried out to determine the best level at which to stop hydrogen absorption. Yields of 66, 70, 74, and 70% of the product (crystallised to constant m. p. from light petroleum, b. p. 60—80°) were obtained when 3·0, 3·2, 3·3, and 3·4 mols. of hydrogen, respectively, were absorbed. In a larger-scale experiment [the diphenylcarbinol (25 g.), glacial acetic acid (100 ml.), platinum catalyst (2·5 g.)] hydrogenation was stopped when 3·3 mols. had been absorbed (20 hours). The yield of product (m. p. 113—115°; light absorption, maximum λ 258·5 mμ., ε 250; hydrochloride, m. p. 255°), after purification by three crystallisations from light petroleum (b. p. 60—80°), was 20·5 g. (80%). In another experiment in which 3·4 mols. of hydrogen were absorbed the yield was 68%. Similar

TABLE II.

Amino-cyclo*hexylcarbinols*, $C_6H_{11}\cdot CR^1(OH)\cdot[CH_2]_n\cdot CHR^2\cdot NR^3R^4$.

No.	R^1.	*n*.	R^2.	NR^3R^4.	Derivative.	M. p.*	Solvent for recrystn.†	Formula.	Analyses. Found, %. C.	H.	N.	Cl/I.	Required, %. C.	H.	N.	Cl/I.
1	Ph	0	H	$N<C_5H_{10}$	*Hydrochloride*	198°	EtOH–Et_2O	$C_{19}H_{29}ON,HCl$	70·2	9·6	4·1	—	70·5	9·3	4·3	—
2	Ph	1	H	NMe_2	*Base*	44—45	Petrol	$C_{17}H_{27}ON$	78·1	10·0	5·7	—	78·2	10·3	5·4	—
					Hydrochloride	211—212 (*d*) [a]	$COMe_2$	—	—	—	—	—	—	—	—	—
3	Ph	1	H	NEt_2	*Base*	50·5—52	Petrol	$C_{19}H_{31}ON$	78·4	10·7	4·7	—	78·9	10·7	4·8	—
					Hydrochloride	184—185 [b]	EtOH–EtOAc	—	—	—	—	—	—	—	—	—
4					*Methiodide*	160—162	EtOH–EtOAc	$C_{20}H_{34}ONI$	—	—	—	29·1	—	—	—	29·4
5	Ph	1	H	$N<C_4H_8$	*Base*	85·5—86·5	Petrol	$C_{18}H_{29}ON$	79·3	10·2	4·8	—	79·4	10·1	4·9	—
					Hydrochloride	226—227 (d)	EtOH–EtOAc	$C_{18}H_{30}ON,HCl$	—	—	—	11·0	—	—	—	11·0
6	—	—	—	—	*Methiodide*	204—205 (d)	EtOH	$C_{20}H_{32}ONI$	—	—	—	29·6	—	—	—	29·6
7	—	—	—	—	*Ethiodide*	158—159 (d)	EtOH–EtOAc	$C_{21}H_{34}ONI$	—	—	—	27·8	—	—	—	28·7
8	Ph	1	H	$N<C_5H_{10}$	Base	114—115 [c]	Petrol ‡	$C_{20}H_{31}ON$	79·7	10·1	4·8	—	79·7	10·3	4·7	—
					Hydrochloride	255 (d) [d]	EtOH	$C_{20}H_{31}ON,HCl$	—	—	—	10·6	—	—	—	10·5
9	—	—	—	—	Methiodide	203—204 [e]	EtOH	$C_{21}H_{34}ONI$	—	—	—	28·4	—	—	—	28·7
10	—	—	—	—	*Ethiodide*	179—180 (d)	EtOH–EtOAc	$C_{22}H_{36}ONI$	—	—	—	27·7	—	—	—	27·8
11	Ph	1	H	$N<C_4H_8O$	Base	114—116 [f]	Petrol	$C_{19}H_{29}O_2N$	75·1	9·6	4·5	—	75·2	9·6	4·6	—
					Hydrochloride	271—272 (d) [g]	EtOH	$C_{19}H_{30}O_2N,HCl$	—	—	—	10·6	—	—	—	10·5
12	—	—	—	—	*Methiodide*	219—220	EtOH–EtOAc	$C_{20}H_{32}O_2NI$	—	—	—	28·3	—	—	—	28·5
13	Ph	1	Me	NMe_2	*Hydrochloride*	198	EtOH–Et_2O	$C_{18}H_{29}ON,HCl$	69·0	9·7	4·7	11·4	69·3	9·6	4·5	11·4
14	Ph	1	Me	$N<C_5H_{10}$	*Hydrochloride*	244—245	EtOH–Et_2O	$C_{21}H_{33}ON,HCl$	71·8	9·3	3·6	—	71·7	9·7	3·8	—
15	Ph	1	Pr^n	NMe_2	*Hydrochloride*	243—244 (d)	EtOH–EtOAc	$C_{20}H_{33}ON,HCl$	70·5	9·9	4·3	10·5	70·7	10·0	4·1	10·5
16	Ph	1	Pr^n	$N<C_5H_{10}$	*Hydrochloride*	262—263 (d)	EtOH–EtOAc	$C_{23}H_{37}ON,HCl$	72·8	9·9	3·6	9·4	72·7	10·0	3·7	9·4
17	Ph	3	H	$N<C_5H_{10}$	*Hydrogen oxalate*	156—157	$COMe_2$	$C_{22}H_{33}ON,C_2H_2O_4$	69·0	8·6	3·5	—	68·7	8·8	3·3	—
18	Ph	4	H	$N<C_4H_8$	*Base*	98	Petrol	$C_{23}H_{35}ON$	—	—	4·3	—	—	—	4·6	—
					Hydrochloride	128	EtOH–Et_2O	$C_{23}H_{36}ON,HCl$	72·1	9·4	3·8	—	72·2	9·8	3·8	—
19	$CH<C_5H_{10}$	0	H	$N<C_5H_{10}$	*Hydrochloride*	208	EtOH–Et_2O	$C_{19}H_{33}ON,HCl$	69·1	10·6	4·1	—	69·2	10·9	4·3	—
20	$CH<C_5H_{10}$	1	H	$N<C_5H_{10}$	*Hydrochloride*	241—242	EtOH–Et_2O	$C_{20}H_{37}ON,HCl$	69·9	11·1	4·2	—	69·9	11·1	4·1	—
21	$CH<C_5H_{10}$	3	H	NEt_2	*Hydrochloride*	130—131	EtOH–Et_2O	$C_{21}H_{41}ON,HCl$	70·2	11·8	3·8	—	70·1	11·7	3·9	—
22	$CH<C_5H_{10}$	3	H	$N<C_4H_8$	*Hydrogen oxalate*	145	$COMe_2$	$C_{21}H_{37}ON,C_2H_2O_4$	67·3	9·9	3·5	—	67·2	10·0	3·4	—
23	$CH<C_5H_{10}$	4	H	$N<C_4H_8$	*Hydrochloride*	146	EtOH–Et_2O	$C_{22}H_{41}ON,HCl$	71·4	11·5	4·1	—	71·1	11·3	3·8	—
24	$CH<C_5H_{10}$	4	H	$N<C_5H_{10}$	*Hydrochloride*	182	EtOH–Et_2O	$C_{23}H_{43}ON,HCl$	71·6	11·4	3·7	9·1	71·6	11·4	3·6	9·2
25	$CH<C_5H_{10}$	5	H	$N<C_5H_{10}$	*Hydrogen oxalate*	138	EtOH–Et_2O	$C_{24}H_{43}ON,C_2H_2O_4$	68·7	10·4	2·9	—	68·9	10·4	3·1	—

[a–e] Denton *et al.* (*loc. cit.*) give m. p.s: (*a*) 210·5—212·5°, (*b*) 186·9—187·4°, (*c*) 114·3—115·0°, (*d*) 258·5°, (*f*) 116·3—117·0°, (*g*) Sublimes >225°. Ruddy and Buckley (*loc. cit.*) give m. p.s: (*a*) 212—213°, (*c*) 114—115°, (*d*) 245—246°, (*e*) 204·5—206·5°.

* (d) = with decomposition. † Petrol = light petroleum (b. p. 40—46°), except ‡ (b. p. 60—80°).

results were obtained when the hydrogenations were carried out at an initial pressure of 67 atm. The speed of hydrogenation was slower when 10% aqueous acetic acid or ethanol was used as solvent, and was faster when the hydrochloride was used in place of the free base.

Compounds 2, 3, and 18 (Table II) were prepared by similar methods.

1-cyclo*Hexyl*-3-*morpholino*-1-*phenylpropan*-1-*ol* (Table II, No. 11). 3-Morpholino-1 : 1-diphenylpropan-1-ol hydrochloride (1·9 g.) (Part I, *loc. cit.*) in ethanol (60 ml.) and water (10 ml.) was shaken with platinum catalyst (0·1 g.) in an atmosphere of hydrogen. The equivalent of 3 mols. of hydrogen was absorbed during 5 days, a white crystalline solid gradually separating. The mixture was warmed on the steam-bath to dissolve the precipitate, filtered hot, concentrated, and allowed to crystallise. The product (1·65 g., 80%) was pure 1-*cyclo*hexyl-3-morpholino-1-phenylpropan-1-ol hydrochloride, m. p. 271—2° (decomp.), from which the base, m. p. 114—116°, was obtained.

Compounds 1 *and* 13—17 (Table II). The corresponding diphenylcarbinol (5·0 g.) was dissolved in glacial acetic acid (20 ml.), platinum catalyst (1·0—1·5 g.) added, and the mixture shaken in an atmosphere of hydrogen until approximately 3·3 mols. had been absorbed. Water was added, the catalyst filtered off, and the filtrate basified with ammonia. The liberated base was extracted with ether, the ethereal solution dried (Na_2SO_4), and the ether evaporated. The residual oil, which did not crystallise on standing, was converted into its *hydrochloride*, which was recrystallised to purity as determined by constancy of m. p. and by absorption spectrum. (The preparation of the diphenylcarbinols required as starting products will be described in subsequent papers.)

1-(4-*Methyl*cyclo*hexyl*)-3-*piperidino*-1-*p*-*tolylpropan*-1-*ol*.—3-*Piperidino*-1 : 1-*di*-*p*-*tolylpropan*-1-*ol* was prepared by reaction of *p*-tolylmagnesium bromide with ethyl β-piperidinopropionate by the general method described in Part I (*loc. cit.*). The base, recrystallised from ethanol, had m. p. 140—141° (Found: C, 81·1; H, 8·7; N, 4·3. $C_{32}H_{39}ON$ requires C, 81·7; H, 9·0; N, 4·3%); *hydrochloride*, recrystallised from ethanol, m. p. 242—243° (decomp.) (Found: Cl, 9·9. $C_{32}H_{39}ON,HCl$ requires Cl, 9·9%).

The di-*p*-tolylcarbinol (4 g.) was dissolved in glacial acetic acid (40 ml.) and shaken in an atmosphere of hydrogen in the presence of platinum catalyst (1·01 g.). Hydrogen absorption ceased when approximately 3 mols. had been taken up. The product, 1-(4-methyl*cyclo*hexyl)-3-piperidino-1-*p*-tolylpropan-1-ol was worked up as the *hydrochloride*, m. p. 242° after recrystallisation from ethanol–ether (Found: C, 71·9; H, 9·4; N, 3·6. $C_{32}H_{45}ON,HCl$ requires C, 72·2; H, 9·8 N, 3·8%).

5-*Bromo*-1-cyclo*hexyl*-1-*phenylpentan*-1-*ol*.—5-Bromo-1 : 1-diphenylpentan-1-ol (15 g.) (to be described in a later paper) was dissolved in ethanol (100 ml.), platinum catalyst (1·5 g.) added, and the mixture shaken in an atmosphere of hydrogen. The speed of hydrogen absorption fell abruptly when 3 mols. of hydrogen had been taken up. The catalyst was filtered off, and the filtrate evaporated under reduced pressure. The residue was warmed on the steam-bath with piperidine (2 mols.). The resulting 5-piperidino-1-*cyclo*hexyl-1-phenylpentan-1-ol was isolated in the usual manner and converted into its hydrogen oxalate (Table II, No. 17).

*Amino-di*cyclo*hexylcarbinols* (Table II, Compounds 19—25).—The corresponding diphenylcarbinols were dissolved in acetic acid and shaken in an atmosphere of hydrogen in the presence of platinum catalyst until the equivalent of 6 mols. of hydrogen had been taken up and absorption had ceased. The products were worked up, as their hydrochlorides or hydrogen oxalates, as described above.

1-*Amino*-3-*phenylalk*-2-*enes* (Table III).—Dehydration of the carbinols to the alkenylamines was carried out by a method which was applied to all cases and is illustrated by the following example. The distilled bases (80—95% yield) were converted into *hydrochlorides* (addition of dry hydrogen chloride to a chloroform solution, followed by ether precipitation) or into *hydrogen oxalates* (addition of oxalic acid to an ethanolic solution, followed by ether precipitation).

3-*Phenyl*-1-*piperidinonon*-2-*ene* (Table III, No. 7).—3-Phenyl-1-piperidinononan-3-ol (12 g.) was dissolved in glacial acetic acid (120 ml.) and concentrated hydrochloric acid (36 ml.), and the solution boiled under reflux for 30 minutes. The solution was concentrated under reduced pressure, and the residue diluted with water and basified with excess of ammonia. The oil which separated was extracted with chloroform, the extract washed with water and dried (Na_2SO_4), and the chloroform evaporated. The residue was distilled under reduced pressure, b. p. 134—136°/0·05 mm.; yield 9·1 g. (80%). Treatment of a chloroform solution of the base with dry hydrogen chloride gave a hydrochloride, m. p. 155—175°; by several recrystallisations from ethanol–ethyl acetate pure 3-*phenyl*-1-*piperidinonon*-2-*ene hydrochloride* (m. p. 212°) was obtained.

Oxidation. Potassium permanganate (4·5 g.) in water (200 ml.) was added dropwise during 1 hour to a solution of the hydrochloride (1·25 g.) in water (20 ml.). The mixture was distilled in steam, and the oil extracted from the distillate by ether. The ethereal extract was dried (Na_2SO_4) and evaporated to give *n*-hexyl phenyl ketone (0·5 g.), b. p. 272°, m. p. 14—15° (lit., b. p. 276°, m. p. 17°) (Found: C, 82·2; H, 9·8. Calc. for $C_{13}H_{18}O$: C, 82·2; H, 9·5%); *p*-nitrophenylhydrazone, m. p. 127—128° (lit., m. p. 127—128°) (Found: C, 70·3; H, 7·5; N, 13·0. Calc. for $C_{19}H_{22}O_2N_3$: C, 70·1; H, 7·1; N, 12·9%).

1-cyclo*Hexyl*-1-*phenyl*-3-*piperidinoprop*-1-*ene* (Table III, No. 11).—Oxidation with aqueous potassium permanganate in a similar manner to that described above gave hexahydrobenzophenone, m. p. 55—56°, after recrystallisation from light petroleum (b. p. 60—80°) (lit., m. p. 59—60°) (Found: C, 83·0; H, 8·6. Calc. for $C_{13}H_{16}O$: C, 83·0; H, 8·5%); semicarbazone, m. p. 174° (lit., m. p. 175°) (Found: N, 17·0. Calc. for $C_{14}H_{19}ON_3$: N, 17·1%).

Phenyl- and cyclo*Hexyl-alkylamines* (Table IV).—The corresponding alkenylamine hydrochloride (5 g.) was dissolved in ethanol (20 ml.) and shaken with 3% palladised charcoal (3·0 g.) in an atmosphere of hydrogen until absorption had ceased. The catalyst was filtered off, the alcohol removed by evaporation, and the residual *hydrochloride* recrystallised to purity. As indicated on p. 54, 1-*cyclo*hexyl-

TABLE III.

1-*Amino*-3-*phenylalk*-2-*enes*, $CPhR^1{:}CH{\cdot}CH_2{\cdot}NR^2R^3$.

No.	R^1.	NR^2R^3.	B. p. of base.	Formula of salt.	M. p. of salt.	Solvent for recrystn. of salt.	Analyses. Found, %. C.	H.	N.	Cl.	Required, %. C.	H.	N.	Cl.
1	Me	NMe_2	122—125°/18 mm.	$C_{12}H_{17}N,HCl$	200—202°	EtOH–$COMe_2$	68·0	8·7	6·5	16·8	68·1	8·5	6·6	16·8
2	Pr[a]	NEt_2	87—95/0·1 mm.	$C_{16}H_{25}N,C_2H_2O_4$	113—119	$COMe_2$	67·1	8·5	4·8	—	67·3	8·4	4·4	—
3	C_5H_{11}[a]	NEt_2	110—115/0·1 mm.	$C_{19}H_{31}N,C_2H_2O_4$	57—60	EtOAc	67·9	8·6	4·0	—	68·8	8·9	4·0	—
4	C_6H_{13}[a]	NEt_2	137—140/0·1 mm.	$C_{21}H_{35}N,C_2H_2O_4$	64—65	EtOAc	70·6	9·2	3·6	—	70·6	9·5	3·6	—
5	CH_2Ph	NEt_2	120—123/0·04 mm.	$C_{20}H_{25}N,HCl$	157—159	EtOH–EtOAc	76·1	8·3	4·3	11·5	76·1	8·2	4·4	11·3
6	Pr[a]	NBu^n_2	123—125/0·1 mm.	$C_{20}H_{33}N,C_2H_2O_4$	90—95	EtOH–Et_2O	69·8	9·2	3·6	—	70·0	9·3	3·7	—
7	C_6H_{13}[a]	$N{<}C_5H_{10}$	134—136/0·05 mm.	$C_{20}H_{31}N,HCl$	212	EtOH–EtOAc	74·4	10·0	4·2	11·0	74·7	10·0	4·3	11·0
8	C_6H_{13}[a]	$N{<}C_5H_6$[b]	110—118/0·02 mm.	$C_{20}H_{29}N,HCl$	221—221·5	EtOH–EtOAc	75·4	9·4	4·4	11·2	75·1	9·4	4·4	11·1
9	C_6H_{13}[a]	$N{<}C_4H_8O$	154—156/0·1 mm.	$C_{21}H_{29}ON,C_2H_2O_4$	125—131	EtOH	67·4	8·5	3·5	—	68·0	8·6	3·5	—
10	$CH{<}C_5H_{10}$	NEt_2	123—125/0·3 mm.[c]	$C_{19}H_{29}N,HCl$	157—160	EtOAc	—	—	4·6	11·6	—	—	4·6	11·5
11	$CH{<}C_5H_{10}$	$N{<}C_5H_{10}$	—	$C_{20}H_{29}N,HCl$	206	EtOH–Et_2O	74·8	9·7	4·5	11·3	75·1	9·4	4·4	11·1
12	$CH{<}C_5H_{10}$[a]	$N{<}C_5H_{10}$	—	$C_{20}H_{33}N,HCl$	230	H_2O	73·6	11·2	4·2	11·3	73·7	11·1	4·3	10·9

[a] Phenyl group of general formula replaced by *cyclo*hexyl. [b] $N{<}C_5H_6$ = 1 : 2 : 5 : 6-Tetrahydropyridino-. [c] Found: C, 84·5; H, 10·3; N, 5·3. $C_{19}H_{29}N$ requires C, 84·1; H, 10·7; N, 5·2%.

TABLE IV.

Phenyl- and cyclo*Hexyl-alkylamines*, $CHR^1R^2{\cdot}[CH_2]_n{\cdot}NR^3R^4$.

No.	*n*.	R^1.	R^2.	NR^3R^4.	Derivative.	M. p. or b. p.	Solvent for recrystn.	Formula.	Analyses. Found, %. C.	H.	N.	Cl.	Required, %. C.	H.	N.	Cl.
1	2	Ph	C_6H_9[a]	$N{<}C_5H_{10}$	*Hydrochloride*	200—201°	EtOH–EtOAc	$C_{16}H_{26}N,HCl$	73·4	10·0	4·7	12·2	73·1	10·2	4·7	12·0
2	2	Ph	C_6H_{13}[a]	$N{<}C_5H_{10}$	*Base*	120—122/0·02 mm.	—	$C_{22}H_{33}N$	83·2	11·6	4·9	—	83·6	11·5	4·9	—
					Hydrochloride	181	EtOH–EtOAc	$C_{22}H_{34}N,HCl$	—	—	4·4	11·2	—	—	4·3	11·0
3	2	Ph	CH_2Ph	NEt_2	*Base*	112—114/0·02 mm.	—	$C_{20}H_{27}N$	85·2	9·8	5·0	—	85·4	9·6	5·0	—
					Hydrochloride	95—97	EtOAc	$C_{20}H_{27}N,HCl$	75·5	8·8	4·5	11·1	75·5	8·8	4·4	11·2
4	2	Ph	$CH{<}C_5H_{10}$	NEt_2	*Base*	190—192/18 mm.	—	$C_{19}H_{31}N$	83·4	11·4	5·3	—	83·5	11·4	5·1	—
					Hydrochloride	125—126	EtOAc	$C_{19}H_{31}N,HCl$	—	—	4·4	11·3	—	—	4·5	11·4
5	2	Ph	$CH{<}C_5H_{10}$	$N{<}C_5H_{10}$	Hydrochloride	222—223[b]	EtOH–Et_2O	$C_{20}H_{31}N,HCl$	74·6	9·9	4·6	—	74·6	10·0	4·4	—
6	2	$CH{<}C_5H_{10}$	$CH{<}C_5H_{10}$	$N{<}C_5H_{10}$	*Hydrochloride*	268—269	EtOH–Et_2O	$C_{20}H_{37}N,HCl$	73·2	11·5	4·2	11·0	73·3	11·6	4·3	10·8
7	4	$CH{<}C_5H_{10}$	$CH{<}C_5H_{10}$	$N{<}C_4H_8$	*Hydrochloride*	180	EtOH–Et_2O	$C_{21}H_{39}N,HCl$	73·7	11·3	4·2	—	73·8	11·7	4·1	—
8	4	$CH{<}C_5H_{10}$	$CH{<}C_5H_{10}$	$N{<}C_5H_{10}$	*Hydrochloride*	222—224	EtOH–Et_2O	$C_{22}H_{41}N,HCl$	73·9	11·4	4·1	—	74·3	11·8	3·9	—

[b] Ruddy and Buckley (*loc. cit.*) give m. p. 227—228°.

1-phenyl-3-piperidinopropane (No. 5) was also prepared by two other routes: (*a*) hydrogenation (4 mols.) of 1 : 1-diphenyl-3-piperidinoprop-1-ene (Part I, *loc. cit.*) in the presence of platinum catalyst, and (*b*) hydrogenation (3 mols.) of 1 : 1-diphenyl-3-piperidinopropane (Part I, *loc. cit.*) in the presence of platinum catalyst. 1 : 1-Di*cyclo*hexyl-3-piperidinopropane (No. 6) was also prepared by hydrogenation (4 mols.) of 1-*cyclo*hexyl-1-phenyl-3-piperidinoprop-1-ene and by hydrogenation (3 mols.) of 1-*cyclo*hexyl-1-phenyl-3-piperidinopropane in the presence of platinum catalyst. 1 : 1-Di*cyclo*hexyl-5-piperidino- and -5-pyrrolidino-pentane (Nos. 7 and 8) were prepared by complete hydrogenation (platinum catalyst) of the corresponding 5-amino-1 : 1-diphenylpentanes (to be described in a later paper).

We are grateful to Mr. A. Bennett for microanalyses.

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12. *The Heterolytic Fission of the Carbon–Iodine Bond in Trifluoroiodomethane.*

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Trifluoroiodomethane reacts with potassium hydroxide, alone or in solution in solvents of high dielectric constant, to give fluoroform, iodine being replaced by a positive iodine mechanism. Nucleophilic substitution of the iodine by OH, NH_2, CN, and NO_2 has so far proved impossible. The exchange reaction between iodide and trifluoroiodomethane in alcoholic solution at 20° has been studied by using radioactive iodide as a tracer. The reaction is of first order with respect to the trifluoroiodomethane and of zero order with respect to the iodide. The rate-determining step at low temperatures is believed to be the heterolysis of the carbon–iodine bond to give a trifluoromethyl anion and an iodine cation.

IT is known that the carbon–iodine bond in trifluoroiodomethane can undergo homolytic fission to give the free perfluoroalkyl radical, CF_3, which can yield organometallic derivatives (Emeléus and Haszeldine, *J.*, 1949, 2948, 2953) and also initiate the polymerisation of olefins (Haszeldine, *J.*, 1949, 2856; *Nature*, 1950, **165**, 152). It has also been found that the iodine in trifluoroiodomethane acts in the presence of solvents of high dielectric constant and strong ionic reagents as if it were positive, and treatment with potassium hydroxide yields fluoroform:

$$\overset{\delta-}{CF_3}\text{–}\overset{\delta+}{I} + KOH \longrightarrow CHF_3 + KOI$$

The reaction of potassium hydroxide is slow in ethereal solution, but, as might be expected, increase in the dielectric constant of the solvent increases the rate. Thus, a rapid and complete destruction of the fluoroiodide is observed in alcohol or acetone at room temperature and fluoroform may be isolated in high yield. The reaction possibly proceeds by attack of a hydroxyl ion on the fluoroiodide, followed either by reaction of the CF_3^- ion with the solvent or with water, or by the decomposition by water of CF_3K formed as intermediate:

$$OH^- + I\text{–}CF_3 \longrightarrow CF_3^- + HOI \xrightarrow{KOH} KOI + H_2O$$

A polymolecular reaction is also possible. If the interpretation of the results of radio-chemical experiments (see below) is correct, however, then CF_3^- ions do not react with alcohol at moderate temperatures. The hypoiodite formed is largely destroyed by reaction with the solvent, and potassium iodide is the main inorganic reaction product. When, however, the fluoroiodide is treated with potassium hydroxide in the absence of a solvent and under conditions such that homolytic fission of the carbon–iodine bond does not occur, potassium iodate and iodide can be detected. Pentafluoroiodoethane (Emeléus and Haszeldine, *loc. cit.*) undergoes analogous reactions with potassium hydroxide and yields pentafluoroethane. Both the fluoroiodides are stable to dilute aqueous alkali at room temperature. Preliminary results have shown that fluoroform is also produced by the slow reaction of trifluoroiodomethane with sodamide in liquid ammonia.

The interaction of trifluoroiodomethane and several of the reagents which will effect nucleophilic substitution of normal alkyl halides—moist silver oxide, potassium phthalimide, metallic cyanides and nitrites—was examined. In no case was the product analogous to that

given by methyl iodide in the same circumstances. The fluoroiodide was resistant to attack by the reagents at lower temperatures, whilst increase in temperature brought about decomposition to ionic fluorine and iodine.

Trifluoroiodomethane (b. p. −22·5°) and pentafluoroidoethane (b. p. 13°) have a conductivity in the pure state of less than 4×10^{-9} ohm^{-1} at −45° and 0°, respectively. Furthermore, on the macro-scale, there is no formation of free iodine when these fluoroiodides are treated with potassium iodide solution, as is the case with inorganic and organic positive iodine compounds. The liquid fluoroiodides are not appreciably ionised, but the existence of ions in alcoholic solution may be deduced from a study of the exchange reaction in this solvent between trifluoroiodomethane and sodium iodide containing radioactive iodine ($CF_3I + Na^{131}I \longrightarrow CF_3{}^{131}I + NaI$). This proves to be a slow reaction at 20°. The rate is independent of the sodium iodide concentration and proportional to the first power of the trifluoroiodomethane concentration, the first-order velocity coefficient being $2{\cdot}6 \times 10^{-6}$ sec.$^{-1}$. The reaction may proceed by the unimolecular ionic mechanism (1), followed by an electron transfer presumably involving I_2 or I_3^- (2), and recombination (3).

$$CF_3I \rightleftharpoons CF_3^- + I^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$I^+ + (^{131}I)^- \rightleftharpoons I_2 \rightleftharpoons I^- + (^{131}I)^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$CF_3^- + (^{131}I)^+ \rightleftharpoons CF_3{}^{131}I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

When the reaction mixture is shaken with mercury at 20°, the rate of exchange is reduced by one-third, whilst the kinetic order is unaffected. This is probably due to the removal by mercury of the molecular iodine postulated as an intermediate in (2). A much faster first-order reaction occurs at temperatures above 80° and involves homolytic fission of the carbon–iodine bond. Preliminary studies on the variation of the rate constant with temperature (−66° to 105°) have shown that below 60° the energy of activation is small, as for an ionic reaction, whilst the reaction above 80° has a much higher activation energy.

The work of Brockway (*J. Physical Chem.*, 1937, **41**, 185, 747) indicated a shortening of the carbon–fluorine and carbon–chlorine bond lengths to 1·36 (±0·02) and 1·73 (±0·02) A. in molecules such as CF_3Cl, CF_2Cl_2, and CHF_2Cl, where two or more fluorine atoms are attached to one carbon atom. This shortening implies a stronger bond between carbon and fluorine and carbon and chlorine, and this is in agreement with the chemical properties of these compounds. Apart from decomposition, they do not show reactions involving the homolytic or heterolytic fission of the carbon–chlorine bond.

It might be expected that the more polarisable the halogen attached to a trifluoromethyl group the more readily would double-bond formation be possible, so that the contribution of canonical forms involving $C{=}X^+$ to the resonance hybrid would decrease in the order $I > Br > Cl > F$. In the case of trifluoroiodomethane the canonical forms (*A*), and particularly (*B*), would therefore contribute appreciably to resonance and shortened and strengthened carbon–fluorine and carbon–iodine bonds would be found.

(*A.*) (*B.*) (*C.*) (*D.*)

Coles and Hughes (*Physical Rev.*, 1949, **76**, 858) report carbon–fluorine and carbon–chlorine bond lengths of 1·32(3) and 1·76(5) A. in CF_3Cl, and these values suggest that it is only the carbon–fluorine bond which is shortened appreciably [cf. methyl fluoride, C–F 1·42 (Brockway, *loc. cit.*), C–F 1·38(4) (Gordy, Simmons, and Smith, *Physical Rev.*, 1948, **74**, 243); methyl chloride, C–Cl 1·77 (Schomaker, quoted by Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46)]. A similar situation is revealed by recent microwave spectroscopic studies on CF_3Br which lead to carbon–fluorine and carbon–bromine bond lengths of 1·32(6) and 1·93(3) A. (Sheridan and Gordy, *Physical Rev.*, 1950, **77**, 292) and 1·32(1) and 1·93(6) A. (Sharbaugh, Pritchard, and Madison, *ibid.*, p. 302) [cf. C–Br in CH_3Br, 1·93(6) (Simmons, Gordy, and Smith, *ibid.*, 1948, **74**, 1246)], and by studies on CF_3I which give a carbon–iodine bond length of 2·16(2), a carbon–fluorine bond length of 1·32(6) being assumed (Sheridan and Gordy, *loc. cit.*) [cf. C–I in CH_3I 2·13(2) (Simmons, Gordy, and Smith, *loc. cit.*)]. It is, therefore, evident that the contribution of canonical forms involving $C{=}X^+$ decreased in the order $F > Cl > Br > I$ (cf. Pauling, " Nature of the Chemical Bond," p. 236).

This is in accord with the reactions of trifluoroiodomethane. The apparent absence of

reactions which involve the nucleophilic replacement of iodine in trifluoroiodomethane does not necessarily mean that the carbon–iodine bond is shorter or stronger, since it can be accounted for by a reversed polarity (C^-I^+) of the carbon–iodine bond, with appreciable contribution to resonance of form (*C*) of a type unimportant in the alkyl halides, and only a slight contribution of form (*D*). The thermal stability of trifluoroiodomethane does not indicate a strong carbon–iodine bond, since the recombination of the trifluoromethyl radical and iodine atom takes place easily; trifluoroiodomethane is known to give a trifluoromethyl radical whereas chlorotrifluoromethane is not.

Experimental.

Conductivity of Liquid Trifluoroiodomethane and Pentafluoroiodoethane.—The conductivities of the fluoroiodides were measured in a cell of 6-ml. capacity with platinum electrodes 15 mm. in diameter and 1 mm. apart, a cathode-ray oscilloscope being used as null-point detector (Haszeldine and Woolf, *Chem. and Ind.*, 1950, **27**, 544). Trifluoroiodomethane at −45·2° and pentafluoroiodoethane at 0° had specific conductivities of $< 4 \times 10^{-9}$ ohm^{-1}.

Reaction of Trifluoroiodomethane and Pentafluoroiodoethane with Alkali.—The reactions described below were carried out in the dark in sealed Pyrex tubes. Fluoroform and pentafluoroethane were identified by molecular-weight and vapour-pressure determinations. (i) No reaction was detected when trifluoroiodomethane was shaken with aqueous sodium hydroxide for 2—3 days. (ii) Trifluoroiodomethane (4·6 g.), potassium hydroxide (5·0 g.), and absolute ethyl alcohol (15 ml.) were shaken for 1 hour and gave an 80% yield of fluoroform. No unchanged fluoroiodide was detected: the alcoholic solution contained potassium iodide but no oxidising agent. With similar quantities, conversion into fluoroform was quantitative at 100°. (iii) Trifluoroiodomethane did not react with ethyl alcohol at room temperature, but when 1·5 g. were heated for 48 hours at 150° with 10 ml. of ethyl alcohol a 19% conversion into fluoroform was obtained. (iv) Pentafluoroiodoethane (1·5 g.), heated with potassium hydroxide (2·0 g.) in ethyl alcohol (25 ml.) for 12 hours at 140°, gave a 74% yield of pentafluoroethane.

Reaction with Potassium Hydroxide in Acetone and Ether.—Potassium hydroxide (3·5 g.) was shaken with trifluoroiodomethane (3·0 g.) and dry acetone (10 ml.) at room temperature. The solution turned brown within a few minutes, and after 0·5 hour all the fluoroiodide had been destroyed and 70% of the theoretical amount of fluoroform had been produced.

Trifluoroiodomethane (3·0 g.), potassium hydroxide (3·0 g.), and dry ether (20 ml.) reacted slowly at room temperature and after 5 days a 30% yield of fluoroform was obtained. When the contents of the reaction tube were acidified, iodine was liberated, and potassium iodate was identified in a repeat experiment.

Reaction with Potassium Hydroxide in the Absence of a Solvent.—Potassium hydroxide pellets (3·0 g.) were crushed and heated in vacuum to remove volatile matter. Trifluoroiodomethane (3·0 g.) was then added, and the reaction tube sealed. After being shaken in the dark at room temperature for 48 hours, the contents of several such tubes were examined: 96% of the fluoroiodide was unchanged and 1% of the theoretical yield of fluoroform was isolated; 60% of the theoretical amount of potassium iodate was present. Repeat experiments gave a 9% yield of fluoroform and an 88% recovery of the fluoroiodide after 15 days' shaking. Potassium iodate was detected qualitatively in the product. The rate of reaction was increased by raising the temperature; for instance, after 30 hours at 90° a mixture of potassium hydroxide (3·0 g.) and trifluoroiodomethane (3·0 g.) gave 7% of the theoretical amount of fluoroform and an 88% recovery of fluoroiodomethane. A radical reaction may be involved in the reactions of 90°. Pentafluoroiodoethane (1·5 g.), shaken with powdered potassium hydroxide in the dark at room temperature for 7 days, gave a 7% yield of pentafluoroethane and an 87% recovery of fluoroiodide.

Attempted Double-decomposition Reactions.—The reaction of trifluoroiodomethane (1·4 g.), potassium cyanide (3·0 g.), and ethyl alcohol (10 ml.) at 160° gave a 61% yield of fluoroform. No trifluoroacetonitrile was isolated. Similar results were obtained with silver cyanide, toluene being used as solvent, and the amount of fluoroform isolated increased as the temperature was raised. Cuprous and mercuric cyanides in absence of a solvent brought about the decomposition of trifluoroiodomethane at elevated temperatures.

With potassium phthalimide (4·5 g.), trifluoroiodomethane (1·5 g.), and toluene (8 ml.) there was little reaction in 12 hours at 180°, and at 220°, although extensive decomposition occurred, no *N*-trifluoromethylphthalimide or primary fluoroamine could be isolated. When trifluoroiodomethane, (2·0 g.) was heated with silver nitrite (3·0 g.) in ether (6 ml.) at 80° the fluoroiodide was unattacked. Reaction occurred at 150° and 200° and some fluoroform was formed by reaction with the ether, but fractionation of the volatile products gave no indication of a compound such as trifluoronitromethane, containing fluorine and nitrogen. In similar experiments, reaction with sodium and potassium methoxides failed to give a fluoro-ether, and with moist silver oxide no trifluoromethanol was obtained.

Exchange Studies, with Radioactive Iodide as a Tracer.—Trifluoroiodomethane is insoluble in water but dissolves readily in absolute ethyl alcohol, in which sodium iodide is also soluble. Radioactive sodium iodide, $Na^{131}I$ (activity 10 μc.), was added to 150 mg. of anhydrous sodium iodide dissolved in ethyl alcohol, and the solution made up to 25 ml. Activities, measured with standard β-counting apparatus, were corrected to zero time in all of the measurements recorded below. A quantity of the sodium iodide solution containing the tracer (referred to as $Na^{131}I$ solution), containing about 30 mg. of sodium iodide in 5 ml. of ethyl alcohol, was sealed with about 40 mg. of trifluoroiodomethane in an 8-ml. Carius tube. Roughly equimolecular proportions of sodium iodide (concentration *b* moles/l.) and trifluoroiodomethane (concentration *a* moles/l.) were then present. The gas-space was kept small so that the greater part of the fluoroiodide was in solution. The tubes were stored in the dark to prevent

photolysis of the fluoroiodide, and, in the experiments in which mercury was added, were shaken vigorously in a vibro-shaker.

After reaction, the trifluoroiodomethane was removed, glass-wool plugs being used to filter the gas and prevent $Na^{131}I$ being carried into the vacuum system as spray. The fluoroiodide and ethyl alcohol (*ca.* 1 ml.), which was simultaneously transferred, were heated in a Carius tube at 100° for 12 hours with alcoholic sodium hydroxide to transform the iodine in the fluoroiodide into sodium iodide. The hydrolysate was neutralised with dilute nitric acid, made slightly alkaline with sodium hydrogen carbonate, and evaporated to dryness. The residue was taken up in 1 ml. of water, centrifuged to remove insoluble matter, and the solution made up to 5 ml. A 0·5-ml. aliquot was acidified with dilute nitric acid and treated with silver nitrate. After coagulation, the silver iodide was centrifuged, washed, and transferred as a slurry to a platinum tray. The water was evaporated and the activity measured. The precipitate was also weighed as a check and losses of 3—8% were found to occur. The β-count was corrected to the theoretical weight of material, based on the weight of trifluoroiodomethane taken. Loss of fluoroiodide as fluoroform was negligible. Standard counting corrections were used throughout.

The reaction may be represented by the equation :

$$\underset{(a-x)}{CF_3I} + \underset{(b-x)}{Na^{131}I} \rightleftharpoons \underset{(x)}{CF_3{}^{131}I} + \underset{(x)}{NaI}$$

The sodium iodide is considered to be uniformly of a low activity, rather than a mixture of active salt and carrier, since its specific activity was constant throughout the series of measurements. In calculating x, allowance was made for the fact that there is a 50% probability that interaction between $^{131}I^-$ and I^+ will produce $^{131}I^+$ and I^-. In all experiments x at the end of the reaction was less than 1% of a and b, and could be neglected in comparison with them. In determining rate coefficients the active mass of NaI, b', was used instead of the concentration b. The activity coefficients of sodium iodide in ethyl-alcoholic solution, derived from the data of Partington and Simpson (*Trans. Faraday Soc.*, 1930, **26**, 625) for the concentrations used (b = 0·02, 0·04, 0·08 mole/l.) are 0·64, 0·57, 0·50, respectively. The results shown in Table I (in which a, b, b', and x are in moles/l.) were obtained at 20°. The rate coefficient k_1 is given by x/at.

TABLE I.

Expt.	CF_3I (counts/min.).	a.	b.	b'.	10^4x.	t (hours).	$10^4dx/dt$.	10^4k_1.
1	828	0·047	0·040	0·0228	281	65	4·33	2·56
2	342	0·047	0·040	0·0228	116	25	4·63	2·74
3	621	0·047	0·040	0·0228	210	50	4·20	2·48
4	1080	0·047	0·040	0·0228	366	85	4·30	2·54
5	178	0·047	0·020	0·0128	603	13	4·64	2·74
6	1287	0·047	0·080	0·0400	436	103	4·23	2·50
7	1030	0·069	0·040	0·0228	348	49	7·11	2·89
8	1262	0·094	0·040	0·0228	427	50	8·54	2·53

Mean $k_1 = 2·62 \times 10^{-4}$.

TABLE II.

Expt.	CF_3I (counts/min.).	a.	b.	b'.	10^4x.	t (hours).	$10^4dx/dt$.	10^4k_1.
9	469	0·047	0·040	0·0228	159	61	2·61	1·54
10	731	0·047	0·040	0·0228	247	85	2·91	1·72
11	835	0·047	0·040	0·0228	283	110	2·58	1·52
12	336	0·047	0·020	0·0128	114	40	2·85	1·69
13	823	0·047	0·081	0·0400	279	100	2·79	1·65
14	1160	0·075	0·040	0·0228	393	83	4·74	1·76
15	1130	0·094	0·040	0·0228	383	65	5·90	1·74
16	1435	0·141	0·040	0·0228	486	61	7·96	1·57

Mean $k_1 = 1·65 \times 10^{-4}$.

In Expts. 1—4, a and b' were constant and t was varied; the plot of x against t is linear (Fig. 1, *A*; the circles show ±5% experimental error). The amount of change x was small, and x/t therefore measured the intial rate and was constant. In Expts. 5—8 the concentrations of CF_3I and $Na^{131}I$ were varied, for, as McKay has pointed out (*Nature*, 1938, **142**, 997), it is impossible to determine the order of an isotopic reaction from a single concentration–time curve, since the concentration remains constant throughout the reaction which then appears to be of first order even if it is in fact bimolecular in mechanism. A plot of log x/t against log b', a being constant in Expts. 1—6, gives a line of nearly zero slope (Fig. 2, *A*). The plot of log x/t against log a, derived from the data of Expts. 1—8, is a line of unit slope, showing the reaction to be of first order with respect to trifluoroiodomethane and independent of the sodium iodide concentration.

The results shown in Table II are for experiments in which the reactants were shaken at 20° with 1 ml. of mercury.

Expts. 9, 10, and 11 have the same constant values of a and b' as in Expts. 1—4, and these values of x and t are plotted in Fig. 1, *B*. The quantity x/t is again constant, but lower than in Expts. 1—4. Expts. 12 and 13 (b' varied, with constant a) and Expts. 9, 10, and 11, which are plotted in Fig. 2, *B*, show the reaction to be of zero order with respect to sodium iodide. Expts. 14, 15, and 16 (a varied, with constant b') and Expts. 9—13 may be used to plot log x/t against log a and yield a line of unit slope, which shows the reaction in presence of mercury to be also of first order with respect to CF_3I. The values of the first-order velocity constant k_1 are included in Tables I and II. Variations in b' do not affect the initial rate. Expts. 5 and 6, and 12 and 13, where a is constant, are plotted on Figs. 1, *A* and 1, *B*.

FIG. 1.

Initial rates.

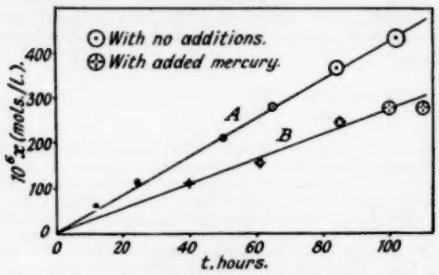
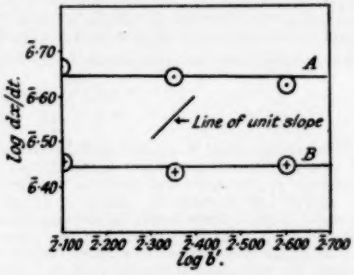


FIG. 2.



The authors are indebted to Dr. A. G. Maddock for his assistance with the radiochemical studies. One of the authors (J. B.) thanks Newnham College, Cambridge, for College and Bathurst Studentships and Imperial Chemical Industries Ltd. for a grant.

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13. 3 : 4-*Benzoxanthens. Part I. The Synthesis and Oxidation of* 3 : 4-*Benzoxanthen.*

By FAWZY G. BADDAR and MUNIR GINDY.

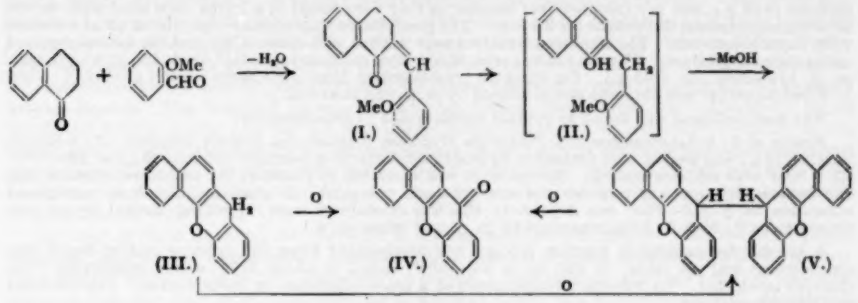
Condensation of *o*-methoxybenzaldehyde with 1-tetralone gives 2-*o*-methoxybenzylidene-1-tetralone. When this is heated with fused potassium hydrogen sulphate–sodium sulphate, there is obtained a mixture of 3 : 4-benzoxanthen and a by-product, most probably 9 : 9′-di-3 : 4-benzoxanthyl. Both compounds are easily oxidised to 3 : 4-benzoxanthone. Careful oxidation of 3 : 4-benzoxanthen gives 9 : 9′-di-3 : 4-benzoxanthyl.

IN an attempt to prepare 8-methoxy-3 : 4-benzofluorene by the cyclisation of 2-*o*-methoxybenzylidene-1-tetralone (I) with phosphoric oxide in xylene (cf. Rapson and Shuttleworth, *J.*, 1940, 638), a very poor yield of a colourless substance, m. p. 90—91°, was obtained. The yield was greatly increased when the cyclisation was effected by fused potassium hydrogen sulphate–sodium sulphate at 260—270° (cf. Baddar and Gindy, *Nature*, 1946, **157**, 409), or better at 230—240° (cf. Gindy, *ibid.*, 1949, **164**, 577). The product was shown to be 3 : 4-benzoxanthen (III), as it gave 3 : 4-benzoxanthone (IV) on oxidation. The cyclisation of (I) to (III) is believed to proceed through the intermediate formation of (II).

Together with 3 : 4-benzoxanthen a by-product, m. p. 230—231°, was obtained which is believed to be 9 : 9′-di-3 : 4-benzoxanthyl (V), resulting from the oxidation of 3 : 4-benzoxanthen by potassium pyrosulphate (formed by the strong heating of potassium hydrogen sulphate). This view is supported by the following facts: (*a*) when a benzene solution of 3 : 4-benzoxanthen and *p*-benzoquinone is exposed to sunlight in a carbon dioxide atmosphere, the same product, m. p. 230—231°, was obtained, (*b*) when 3 : 4-benzoxanthen was heated with potassium hydrogen sulphate–sodium sulphate at 260—270° for ½ hour, it was partly converted into 3 : 4-benzoxanthone, 9 : 9′-di-3 : 4-benzoxanthyl, and a thermochromic substance melting above 317°, and (*c*) when the product, m. p. 230—231°, was oxidised with atmospheric oxygen in sunlight it gave 3 : 4-benzoxanthone.

The attempted synthesis of 9 : 9′-di-3 : 4-benzoxanthyl (V) through an Ullmann condensation

of 9-bromo-3 : 4-benzoxanthen failed, as attempts to prepare this bromo-compound by the action of dry hydrogen bromide on 3 : 4-benzoxanthhydrol (cf. Gomberg and Cone, *Annalen*, 1910, **376**, 192) resulted in the isolation of 3 : 4-benzoxanthone.



Experimental.

(M.p.s are not corrected. Microanalyses are by Drs. Weiler and Strauss, Oxford.)

2-o-*Methoxybenzylidene*-1-*tetralone* (I).—A mixture of freshly distilled *o*-methoxybenzaldehyde (13·6 g., 1 mol.) and 1-tetralone (14·6 g., 1 mol.) was treated with 4% alcoholic potassium hydroxide (100 c.c.), and the mixture was left overnight, neutralised with acetic acid, and diluted with water until the solution became turbid. The precipitated product was filtered off, washed thoroughly with cold alcohol, and dried. It had m. p. 107—108° (yield, 25 g., 95%). On crystallisation from alcohol 2-o-*methoxybenzylidene*-1-*tetralone* was obtained in light-yellow crystals, m. p. 110—111° (Found : C, 81·6; H, 6·1. $C_{18}H_{16}O_2$ requires C, 81·1; H, 6·1%). It was soluble in concentrated sulphuric acid giving an orange-red solution.

3 : 4-*Benzoxanthen* (III).—A well powdered mixture of potassium hydrogen sulphate (60 g.) and sodium sulphate (15 g.) was melted and thoroughly stirred. 2-o-Methoxybenzylidene-1-tetralone (20 g.) was then added in one lot, and the mixture heated at 230—240° for ¾ hour, and, after cooling, extracted with hot water, and the product was filtered off, dried, and then extracted with benzene. The benzene extract on being kept deposited a by-product, m. p. 210—225°, which was removed. Evaporation of the solvent left a tarry, dark residue, which was purified by repeated vacuum-distillation (b. p. 210°/3 mm.). It was crystallised from alcohol giving 3 : 4-*benzoxanthen* (7·1 g., 40%), m. p. 90—91° [Found : C, 88·4; H, 5·3%; *M* (Rast), 236. $C_{17}H_{12}O$ requires C, 87·9; H, 5·2%; *M*, 232]. It was soluble in hot alcohol and most organic solvents. The *picrate*, prepared in alcohol, formed red needles, m. p. 125—126°, from alcohol (Found : C, 59·8; H, 3·4; N, 9·1. $C_{17}H_{12}O,C_6H_3O_7N_3$ requires C, 59·9; H, 3·3; N, 9·1%). It was soluble in alcohol and acetone, difficulty soluble in benzene; it decomposed when heated with light petroleum.

A poorer yield of benzoxanthen was obtained when the reaction was carried out at 260—270°; efficient stirring was essential. Attempted cyclisation of 2-o-methoxybenzylidene-1-tetralone by means of phosphoric oxide in xylene (cf. Rapson and Shuttleworth, *loc. cit.*) gave a very poor yield of 3 : 4-benzoxanthen.

The by-product, m. p. 210—225°, was purified by repeated crystallisation from chloroform–ethyl alcohol giving 9 : 9′-*di*-3 : 4-*benzoxanthyl* (V) in needles, m. p. 230—231° [Found : C, 88·7; H, 5·1%; *M* (Rast), 404. $C_{34}H_{22}O_2$ requires C, 88·3; H, 4·8%; *M*, 462.]

Oxidation of 3 : 4-*Benzoxanthen to* 3 : 4-*Benzoxanthone.*—In all cases the product was crystallised from methyl alcohol or dilute acetone, and identified by m. p. and mixed m. p. with an authentic specimen prepared as described by Knapp (*J. pr. Chem.*, 1936, **146**, 116).

(*a*) *With potassium permanganate.* To a warm (40—50°) solution of 3 : 4-benzoxanthen (2 g.) in acetone (50 c.c.) and water (20 c.c.), powdered potassium permanganate (2·8 g.) was added portionwise at such a rate that the temperature did not exceed 50°. The manganese dioxide was removed by sulphur dioxide, and the acetone evaporated. The precipitate was filtered off and crystallised, giving 3 : 4-benzoxanthone (*ca.* 1·6 g.) in needles, m. p. 160—161° [Found : C, 82·9; H, 4·2%; *M* (Rast), 250. Calc. for $C_{17}H_{10}O_2$: C, 82·9; H, 4·1%; *M*, 246].

(*b*) *With selenium dioxide.* A mixture of 3 : 4-benzoxanthen (2 g.), selenium dioxide (4 g.), and water (4 c.c.) was heated in a sealed tube at 230—240° for 4 hours. The contents of the tube were filtered and the product was purified as stated above, and proved to be 3 : 4-benzoxanthone (1·9 g.).

(*c*) *With atmospheric oxygen.* A solution of 3 : 4-benzoxanthen (0·2 g.) in dry thiophen-free benzene (15 c.c.) or chloroform (15 c.c.) was exposed in a Pyrex tube to sunlight for 3—5 days (September). Evaporation of the solvent left a product which was identified as 3 : 4-benzoxanthone.

(*d*) *With* p-*benzoquinone.* A solution of 3 : 4-benzoxanthen (0·2 g.) and *p*-benzoquinone (0·2 g.) in benzene was exposed to sunlight for a few hours. The precipitated quinhydrone was filtered off, and the filtrate evaporated to dryness. The residue was repeatedly crystallised from dilute acetone to give 3 : 4-benzoxanthone.

Oxidation of 3 : 4-benzoxanthen to 3 : 4-benzoxanthone could also be effected by means of alkaline ferricyanide at 80—90° or potassium dichromate in cold or boiling acetic acid. Hydrogen peroxide, however, failed to effect this oxidation.

Oxidation of 3 : 4-*Benzoxanthen to* 9 : 9′-*Di*-3 : 4-*benzoxanthyl.*—3 : 4-Benzoxanthen (0·4 g.), *p*-benzoquinone (0·08 g.), and dry thiophen-free benzene (5 c.c.) were sealed in a Pyrex tube filled with carbon dioxide, and exposed to sunlight for 3 hours. The precipitated quinhydrone was filtered off and washed with warm chloroform. The combined solutions were washed with dilute alkali, and the solvent removed under reduced pressure. The residue was crystallised from chloroform–methyl alcohol to give a product, m. p. 175—200° (*ca.* 0·05 g.). On repeated crystallisation from chloroform–methyl alcohol, 9 : 9′-di-3 : 4-benzoxanthyl was obtained and identified by m. p. and mixed m. p.

The mother-liquor was found to contain unchanged 3 : 4-benzoxanthen.

Fusion of 3 : 4-*Benzoxanthen with Potassium Hydrogen Sulphate and Sodium Sulphate.*—3 : 4-Benzoxanthen (2 g.) was heated with potassium hydrogen sulphate (20 g.)–sodium sulphate (5 g.) at 260—270° for ½ hour with efficient stirring. The product was extracted as stated in the second experiment, and the benzene solution was concentrated and set aside overnight. A small amount of an amorphous substance, m. p. 210—220°, was deposited; this was crystallised from chloroform–methyl alcohol and proved to be 9 : 9′-di-3 : 4-benzoxanthyl by m. p. and mixed m. p.

A second thermochromic fraction (0·2 g.) was precipitated when the benzene mother-liquor was concentrated and set aside; it had m. p. 254—260°, raised to above 317° on recrystallisation from chloroform–alcohol. Its toluene solution acquired a green coloration on being heated, This material is under investigation.

Unchanged 3 : 4-benzoxanthen and 3 : 4-benzoxanthone were identified in the residual solid obtained by evaporation of the benzene.

Action of Hydrogen Bromide on 3 : 4-*Benzoxanthhydrol.*—Dry hydrogen bromide was bubbled into a suspension of 3 : 4-benzoxanthhydrol (Werner, *Ber.*, 1901, **34**, 3303) in glacial acetic acid. The saturated solution was set aside for 3 hours and then filtered from a small amount of a red compound. The product was precipitated with water and extracted with benzene. The benzene was evaporated and the residue crystallised from light petroleum (b. p. 60—80°) to give a crystalline product which was proved to be 3 : 4-benzoxanthone by m. p. and mixed m. p.

Oxidation of 9 : 9′-*Di*-3 : 4-*benzoxanthyl with Atmospheric Oxygen.*—A solution of 9 : 9′-di-3 : 4-benzoxanthyl (0·05 g.) in chloroform (5 c.c.) was exposed to sunlight for 3 days (September). The solvent was evaporated and the product was crystallised from methyl alcohol to give 3 : 4-benzoxanthone, identified by m. p. and mixed m. p.

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14. *The* Senecio *Alkaloids. Part VIII. The Occurrence and Preparation of the* N*-Oxides. An Improved Method of Extraction of the* Senecio *Alkaloids.*

By MATTHEUS J. KOEKEMOER and FRANK L. WARREN.

The preparation and properties of the *N*-oxides of platyphylline, platynecine, and rosmarinine are described.

The occurrence of the *Senecio* alkaloids as *N*-oxides, or their tautomeric forms, is indicated. An improved method of isolation of the alkaloids involving their reduction before isolation is developed to give yields several times greater than those previously reported.

ISATIDINE, first isolated from *Senecio isatideus* (Blackie, *Pharm. J.*, 1937, **138**, 102), and since found associated with retrorsine in various *Senecio* species (de Waal, *Onderstepoort J. Vet. Sci. and Animal Ind.*, 1939, **12**, 155; de Waal and Pretorius, *ibid.*, 1941, **17**, 181), has been shown by Christie, Kropman, Leisegang, and Warren (*J.*, 1949, 1700; cf. also Leisegang and Warren, *J.*, 1949, 486; 1950, 702) to be retrorsine *N*-oxide. Isatidine is insoluble in chloroform, which is the solvent usually employed for the extraction of the *Senecio* alkaloids, and its initial detection and later isolation in smaller quantities from the other species were facilitated by its ready crystallisation from aqueous concentrates.

The aqueous solutions left after removal of the chloroform-soluble alkaloids from several *Senecio* species investigated in these laboratories have always given pronounced tests for alkaloids. The evaporation, however, of the aqueous moiety was always associated with extensive decomposition, and butanol extraction gave only gummy products. Retrorsine is the only *Senecio* alkaloid which is known to exist as its *N*-oxide (isatidine), and the authors set out to find whether the other alkaloids also occurred in the oxidised form in the plant.

To facilitate this study the *N*-oxides of platyphylline, platynecine, and rosmarinine were prepared by oxidation of the bases with hydrogen peroxide (cf. Christie *et al.*, *loc. cit.*); platyphylline *N*-oxide, m. p. 180—184°, and platynecine *N*-oxide, m. p. 217—218°, were crystalline solids, whilst rosmarinine *N*-oxide was obtained only as an amorphous powder. The structures of these compounds follow from the summary of the structures of the *Senecio* alkaloids given by Leisegang and Warren (*J.*, 1950, 702). That these *N*-oxides of platyphylline and rosmarinine have not been isolated previously from the plant is readily understood in view of their insolubility in chloroform whilst their hygroscopic nature prevents crystallisation from the aqueous mother-liquors. The isolation by way of the phosphotungstate, employed successfully by de Waal and Pretorius (*loc. cit.*) for the isolation of small quantities of retrorsine *N*-oxide, is not practicable in view of the difficulty of crystallisation, particularly of mixtures with the amorphous rosmarinine *N*-oxide. On the other hand, these *N*-oxides in dilute hydrochloric acid were readily reduced (cf. Leisegang and Warren, *loc. cit.*) by zinc dust to give the original alkaloids in quantitative yield.

In view of these findings, the alkaloids in a number of *Senecio* species were re-investigated. For this purpose, the usual alcohol extraction was effected in glass apparatus, and the chloroform-soluble alkaloids were first completely removed. The residual aqueous solution was then reduced with zinc dust in acid solution, made alkaline again, and re-extracted with chloroform. The results from a representative number of extractions are shown in the table, which gives the percentages of impure and purified alkaloids based on the dried plant material.

In all the *Senecio* species investigated, the chloroform extract after reduction gave alkaloids in purer form, as revealed by the quantity of pure alkaloids obtained from the impure base, and in considerably larger yield than the first chloroform extraction. When no alkaloids were obtained in the first chloroform extract, none were obtained after reduction, *e.g.*, in *S. panduri-folius*; and the same alkaloids were obtained before and after reduction. These findings indicate that the *Senecio* alkaloids exist in the plant mainly as the *N*-oxide form but seemingly always associated with a smaller quantity of unoxidised alkaloid.

For the routine isolation of alkaloids, the reduction of the defatted aqueous solutions can be effected directly and the total alkaloids extracted in one operation. The enormous increase in yield by this new method should greatly facilitate constitutional studies which have been limited by availability of material. *S. coronatus* yielded only traces of alkaloid soluble in chloroform; but the new method of reduction before isolation has now given increased yields of alkaloid commensurate with its toxic nature.

Plant.	Alkaloid.	Before reduction.	After reduction.
S. isatideus D.C. (ii)	Crude	0·2—0·4%	4—5%
	retrorsine	0·1—0·2	3·5—4
S. adnatus D.C. (i)	Crude	0·63	3·2
	rosmarinine	0·25	2·2
S. hygrophilus D. and S. (i)	Crude	1·0	2·7
	rosmarinine	0·2	0·55
	platyphylline	0·2—0·4	1·5—1·7
S. brachypodus D.C. (i)	Crude	0·3	1·0
	rosmarinine	0·15	0·7

For original identification of the alkaloids from these plants cf. (i) Richardson and Warren, *J.*, 1943, 453, (ii) Blackie, *loc. cit.*

This widespread occurrence of the alkaloid *N*-oxides in the *Senecio* species (Compositæ) probably has its counterpart in the other genera, *Cynoglossum*, *Heliotropium*, *Trichodesma* (Boraginaceæ), and *Crotalaria* (Leguminosæ–Papilionaceæ) which contain similar pyrrolizidine alkaloids (cf., respectively, Menschikov, *J. Gen. Chem. Russia*, 1948, **18**, 1736; *Ber.*, 1932, **65**, 974; Menschikov and Borodina, *J. Gen. Chem. Russia*, 1945, **15**, 225; Adams and Rogers, *J. Amer. Chem. Soc.*, 1939, **61**, 2815, *et seq.*). The recent isolation by Galinovski, Goldberger, and Pohm (*Monatsh.*, 1949, **80**, 550) of laburnine, hydroxymethylpyrrolizidine, from *Cytisus laburnum* (Leguminosæ–Papilionaceæ) connects these tertiary amines with the lupinane group of alkaloids, and the natural occurrence of *N*-oxides, or their tautomeric forms, is probably more widespread than previously envisaged.

Experimental.

Analyses are by Drs. Weiler and Strauss, Oxford. All m. p.s are uncorrected.

Preparation of N-Oxides.—The alkaloid was oxidised by hydrogen peroxide as previously reported for the conversion of retronecine into isatinecine (Leisegang and Warren, *J.*, 1949, 486; cf. also Christie,

Kropman, Leisegang, and Warren, *J.*, 1949, 1700). The excess of hydrogen peroxide was destroyed by platinum as described by Cope, Foster, and Towle (*J. Amer. Chem. Soc.*, 1949, **71**, 3929).

Platyphylline N-oxide. The product, crystallised from alcohol–acetone by cooling the solution to 0° or by the addition of ether, gave *platyphylline N-oxide* as fine, silky needles, m. p. 180—184° (decomp.), $[\alpha]_D^{18}$ −59° (c = 0·9 in water), which appear to lose solvent of crystallisation on being heated. The very hygroscopic crystals were dried at 78° in a high vacuum for analysis (Found: C, 60·9; H, 7·9; N, 4·0. $C_{18}H_{27}O_6N$ requires C, 61·2; H, 7·7; N, 4·0%). Reduction of platyphylline *N*-oxide with zinc and hydrochloric acid, and extraction of the alkaline solution with chloroform gave platyphylline, m. p. 124—126° undepressed when mixed with authentic specimen (cf. the reduction of isatidine, Christie, Kropman, Leisegang, and Warren, *J.*, 1949, 1700).

Platynecine N-oxide. The product, crystallised from alcohol–acetone, gave *platynecine N-oxide* in stout, monoclinic, hygroscopic prisms, m. p. 217—218° (decomp.), which were dried at 78° in a high vacuum for analysis (Found: Loss of weight on heating, 23·1. $C_8H_{15}O_3N,2\frac{1}{2}H_2O$ requires H_2O, 20·6. $C_8H_{15}O_3N,C_2H_5OH$ requires C_2H_5OH, 21·1%) (Found: C, 53·7; H, 8·6; N, 7·9. $C_8H_{15}O_3N$ requires C, 55·5; H, 8·7; N, 8·1%). The *picrate* crystallised from absolute alcohol in needles, m. p. 160—162° (Found: C, 42·05; H, 4·6; N, 13·6. $C_{14}H_{18}O_{10}N_4$ requires C, 41·8; H, 4·5; N, 13·9%). Platynecine *N*-oxide was reduced as above, and the solution made alkaline with sodium carbonate, filtered, evaporated to dryness in a vacuum, and extracted with chloroform; this gave platynecine, m. p. 146—148° undepressed when mixed with authentic specimen.

Rosmarinine N-oxide. This was obtained as a syrup which in a vacuum gave a hygroscopic, amorphous solid which could not be induced to crystallise and decomposed in a vacuum at 169°. The picrate was amorphous. Reduction of rosmarinine *N*-oxide, as described for platyphylline *N*-oxide, gave rosmarinine, m. p. 204—206° undepressed when mixed with authentic specimen.

Extraction of Alkaloids.—The dried ground plant material (1 kg.) was refluxed with alcohol (3 l.), the solution decanted, and the residue pressed out. This operation was repeated twice more. The alcohol was evaporated under reduced pressure, water (300 ml.) added, and the residual alcohol removed under reduced pressure. The concentrate was treated with 17% aqueous citric acid (200 ml.), the fats filtered off, and the filtrate extracted with ether. The aqueous solution was made alkaline with ammonia solution and extracted with chloroform (8 × 150 ml.). The solution was made acid with 11N-hydrochloric acid (200 ml.) and treated with zinc dust (30 g.), and the solution filtered, made alkaline with 14N-ammonia (200 ml.), and re-extracted with chloroform (8 × 150 ml.).

The authors acknowledge a grant for equipment and a bursary to one of them (M. J. K.) from the South African Council for Scientific and Industrial Research.

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15. *The Conductivities of Some Complex Cobalt Chlorides and Sulphates.*

By I. L. Jenkins and C. B. Monk.

From the conductivities of dilute solutions at 25° of the chlorides and sulphates of hexamminocobalt, trisethylenediaminocobalt, and trispropylenediaminocobalt, the limiting mobilities of the cobaltic cations, and the dissociation constants of the ion pairs formed between these and chloride and sulphate ions have been determined. The increasing radii of the complex cations are found to alter systematically the limiting mobilities of these ions and the dissociation constants of their sulphates. A comparison is drawn between the sizes of these ion pairs as calculated by Stokes's law and by Bjerrum's method.

Among the various factors which influence the extent to which ions associate in solution is their effective size. This may be seen, for instance, by a comparison of similar salts containing organic ions in non-aqueous solvents, where the dissociation constants are found to increase with increasing size of the organic ions (Kraus and Fuoss, *J. Amer. Chem. Soc.*, 1933, **55**, 3614; Davies, "Conductivity of Solutions," 1933, Chap. 18). In aqueous solutions, hydration effects distort this generalisation. So far as quantitative relations are concerned, Bjerrum (*Kgl. Danske Vidensk. Selskab.*, 1926, **7**, No. 9) has proposed, for those cases where the forces are essentially polar, the relation

$$K^{-1} = \frac{4\pi N}{1000}\left(\frac{|z_1 z_2|}{DkT}\right)^3 Q(b) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $b = (|z_1 z_2|)^2/aDkT$; a represents the distance of closest approach of the ions forming

the ion pair. Generally, this has been used to calculate values of a from experimentally found dissociation constants, when from the calculated values of $Q(b)$, b can be obtained from tables (Bjerrum, *loc. cit.*) and hence a found. Alternatively, by assuming a, as found from data with aqueous solutions, to be constant, one can compare the variation of K with variations in the dielectric constant D when this is altered by the addition of various organic solvents to water. This implies that the extent of ion-hydration remains constant, but the agreement with experimentally found results appears to be fairly good with large ions such as lanthanum ferricyanide (James, *J.*, 1950, 1094).

The sizes of ions, when they are of similar character, also cause variations in their mobilities. This may be seen for instance with the polydecylamine salts (Ralston and Hoerr, *J. Amer. Chem. Soc.*, 1942, **64**, 773) and some simple aliphatic anions (Bredig, *Z. physikal. Chem.*, 1894, **13**, 191). A development of this aspect of mobilities is the well-known instance of the alkali-metal cations where the mobilities are in inverse order to the radii of the bare ions owing to the effective radii of the hydrated ions being in the order Li > Na, etc., which is the order of increasing mobilities.

A quantitative relation between ion mobilities and their radii is expressed by Stokes's law

$$v = Xze/6\pi\eta a$$

which, in terms of conductivity in aqueous solution at 25°, becomes

$$a = 9{\cdot}16 \times 10^{-7} z/\Lambda_i^\circ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

a being the ion radius of valency z and limiting ionic mobility Λ_i°. With small ions whose radii are of the same order of magnitude as the solvent molecules, it is doubtful if the solvent viscosity truly describes the retarding effect. Furthermore, hydration effects introduce additional complications. With large spherical ions we would expect solvation effects to be much smaller, owing to the low density of charge on their surfaces, and we would have conditions more favourably suited to the requirements of Stokes's law. With this in mind, we have followed the conductivities of the chlorides and sulphates of some rather large symmetrical complex cobalt ions, which gradually increase in size. The chlorides enable the limiting ion mobilities, Λ_i°, to be found and their radii to be calculated from (2). With the sulphates, the dissociation constants of the ion pairs have fairly low values, and from these, Bjerrum's expression gives values of a which may be compared with those derived from Stokes's law.

Experimental.

The conductivity equipment and the determination of the cell constants have been described in earlier papers (Davies, *J.*, 1937, 432; Davies and Monk, *J.*, 1949, 413). All the measurements were at 25° ± 0·01°. Hexamminocobalt(III) chloride, $Co(NH_3)_6Cl_3$, was prepared by the method of Bjerrum and Reynolds ("Inorganic Syntheses," McGraw-Hill, 1946, Vol. II, Chap. 8). The crystals were thoroughly washed with conductivity water and absolute alcohol, then dried to constant weight over phosphoric oxide and paraffin wax in a vacuum. The stock solutions were made up by weight, buoyancy corrections being applied. The resistance readings, when the cell was not disturbed, were found to drift slowly, but on shaking the cell fairly vigorously the original readings could always be reproduced. This effect, which is undoubtedly one of adsorption on the electrodes, was also noticed by Hartley and Donaldson (*Trans. Faraday Soc.*, 1937, **33**, 457) in their conductivity measurements with this salt; they attempted a time extrapolation to obtain the correct readings.

Trisethylenediaminocobalt(III) chloride was formed by Work's method ("Inorganic Syntheses," Vol. II, Chap. 8). The crystals were dissolved in water and reprecipitated by addition of pure ethyl alcohol. This was repeated several times, and the product dried in a vacuum oven at 50—60°. The salt was slightly hygroscopic, so the stock solutions were made up approximately by weight, and the exact concentrations found gravimetrically as silver chloride; the duplicates of these agreed to within ±0·03%. These solutions had a pH of >6. Resistance readings were constant, adsorption effects being very slight.

Trispropylenediaminocobalt(III) chloride was prepared as follows. 11·6 Ml. of specially pure B.D.H. propylenediamine were diluted to 40 ml. with water and partly neutralised with 5·3 ml. of concentrated hydrochloric acid in 17 ml. of water. This mixture was poured into a solution of 5·3 g. of hydrated cobalt chloride in 17 ml. of water. Oxygen was bubbled through rapidly for 3 hours. The solution was evaporated to about 15 ml., then 4 ml. of concentrated hydrochloric acid and 30 ml. of ethyl alcohol were added to precipitate the salt. This was washed with alcohol until the washings had a pH of >6, then dried in a vacuum desiccator over phosphoric oxide and paraffin wax. The concentrations of the stock solutions were determined gravimetrically as above. A slight drift in the resistance readings when the cell was left stationary was readily overcome by shaking the cell before taking readings.

Hexamminocobalt(III) *sulphate.* This was prepared by dissolving 27 g. of hydrated cobalt sulphate and 15 g. of ammonium sulphate in 20 ml. of water, adding 0·5 g. of activated decolorising animal

charcoal as catalyst, and 50 ml. of concentrated ammonia solution, then drawing air through the solution for 5 hours. The product was filtered off, dissolved, and the animal charcoal filtered off, the sulphate being precipitated by addition of 100 ml. of concentrated sulphuric acid and cooling to 0°. It was washed with water, dissolved in water, and precipitated with alcohol, this process being repeated six times. Although the salt was dried in a vacuum oven at 50°, it could not be brought to constant weight, being slightly hygroscopic. Consequently, the concentrations of the stock solutions were found by quantitative sulphate analysis. Vogel's method ("Quantitative Analysis," Longmans, Green and Co., p. 478) was used, the barium sulphate being weighed in sintered porcelain crucibles; duplicates agreed to within ±0·03%. The stock solutions had a pH of *ca.* 6. Adsorption effects were very small, and it was easy to get consistent resistance readings.

TABLE I.

10^4C.	$10^2C^{\frac{1}{2}}$.	Λ.	$\Lambda + bC^{\frac{1}{2}}$.	α.	$10^3\kappa$.	10^4C.	$10^2C^{\frac{1}{2}}$.	Λ.	$\Lambda + bC^{\frac{1}{2}}$.	α.	$10^3\kappa$.
(i) *Conductivity of hexamminocobalt*(III) *chloride solutions.*											
1·5374	1·240	171·44	175·33	0·9970	45	6·6539	2·578	166·29	174·38	0·9840	32
2·2421	1·498	170·46	175·16	0·9947	38	7·0800	2·661	165·85	174·19	0·9817	29
2·7957	1·670	169·75	174·99	0·9928	33	7·9998	2·828	165·35	174·12	0·9819	33
4·4657	2·113	168·10	174·73	0·9891	33	8·4888	2·915	164·93	174·07	0·9799	31
4·5705	2·138	168·03	174·74	0·9892	34	9·4439	3·070	164·20	173·83	0·9767	29
5·7812	2·405	166·94	174·48	0·9857	31						
(ii) *Conductivity of trisethylenediaminocobalt*(III) *chloride solutions.*											
2·1450	1·465	146·33	150·71	0·9917	22	5·8170	2·412	142·80	150·01	0·9779	18
2·3865	1·545	145·83	150·45	0·9876	16	6·1207	2·474	142·44	149·84	0·9749	17
2·5895	1·609	145·52	150·33	0·9854	15	7·2284	2·689	141·72	149·76	0·9729	20
3·4420	1·855	144·89	150·44	0·9864	21	7·8923	2·809	141·23	149·63	0·9704	18
3·8508	1·962	144·38	150·25	0·9838	18	10·090	3·177	139·79	149·29	0·9634	19
4·4106	2·100	144·00	150·28	0·9834	21	10·143	3·185	139·86	149·38	0·9647	20
5·4216	2·328	142·95	149·91	0·9767	18	12·158	3·487	138·63	149·06	0·9584	20
(iii) *Conductivity of trispropylenediaminocobalt*(III) *chloride solutions.*											
1·9246	1·387	137·18	141·01	0·9929	23	6·5440	2·558	133·31	140·36	0·9813	27
2·2269	1·492	136·93	141·04	0·9936	30	7·4520	2·730	132·50	140·03	0·9751	22
3·5599	1·887	135·48	140·68	0·9873	23	8·3983	2·898	132·05	140·04	0·9750	24
4·3626	2·087	134·93	140·69	0·9872	27	9·0360	3·006	131·57	139·82	0·9710	22
5·9195	2·433	133·77	140·48	0·9835	28	10·115	3·180	131·05	139·82	0·9709	24

10^4C.	$10^2C^{\frac{1}{2}}$.	Λ.	$10^3\kappa$.	$10^4\kappa$.	10^4C.	$10^2C^{\frac{1}{2}}$.	Λ.	$10^3\kappa$.	$10^4\kappa$.
(iv) *Conductivity of hexamminocobalt*(III) *sulphate solutions.*									
0·755	0·869	161·04	0·239	2·80	5·384	2·320	123·12	5·96	2·71
1·483	1·218	150·99	0·769	2·80	8·406	2·899	113·65	10·94	2·84
2·557	1·599	140·44	1·84	2·79	9·033	3·006	110·55	12·36	2·72
3·335	1·826	134·57	2·88	2·75	12·70	3·564	103·18	19·38	2·78
4·369	2·090	128·16	4·36	2·73	14·84	3·852	99·22	23·88	2·75
4·671	2·161	126·85	4·79	2·75					
(v) *Conductivity of trisethylenediaminocobalt*(III) *sulphate.*									
1·278	1·130	136·32	0·457	3·88	8·604	2·932	101·16	10·5	3·25
3·048	1·746	124·11	1·95	3·92	9·082	3·013	103·74	10·3	3·65
3·584	1·893	117·74	2·92	3·18	10·68	3·208	97·11	14·1	3·29
4·667	2·160	116·13	3·88	3·96	13·12	3·623	91·89	19·1	2·94
6·141	2·480	111·18	5·82	3·86					
(vi) *Conductivity of trispropylenediaminocobalt*(III) *sulphate.*									
1·858	1·363	133·77	0·240	16·6	7·847	2·801	120·98	2·49	19·1
2·407	1·551	132·78	0·306	21·0	7·993	2·827	119·74	2·86	16·9
3·662	1·914	129·02	0·698	19·2	9·541	3·089	117·48	3·76	17·0
4·924	2·219	126·32	1·14	19·5	11·27	3·357	116·23	4·46	18·9
5·733	2·394	124·02	1·62	17·5	14·61	3·826	112·56	6·61	19·0

Trisethylenediaminocobalt(III) *sulphate.* 61 Ml. of 70% ethylenediamine in water were partly neutralised with 1·5 ml. of concentrated sulphuric acid in 10 ml. of water. To this, a solution of 24 g. of cobalt sulphate in 75 ml. of water was added, and a vigorous stream of air passed through for 5 hours. The mixture was evaporated on a water-bath until a crust formed on the surface. On addition of 15 ml. of concentrated sulphuric acid and 30 ml. of ethyl alcohol, the salt was precipitated. It was filtered off and washed with alcohol until the washings were colourless. The sulphate was recrystallised by dissolving it in water and adding alcohol, this process being repeated five times. The stock solutions were analysed gravimetrically as in the previous case, duplicates agreeing within ±0·03%. The stock solutions had a pH of *ca.* 4, which in spite of the numerous recrystallisations was probably due to traces of free acid. In place of the usual solvent correction, a pH–concentration curve was obtained and the pH's of the solutions whose resistances were measured were obtained by interpolation. Since hydrogen

ions contribute to the major part of the solvent conductivity, and the specific conductivity due to these is given by $\kappa = 350[H^+] \times 10^{-9}$, where 350 is the mobility of the ion (Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold, New York, 1943, p. 172), this amount was subtracted from the measured specific conductivities before calculation of the equivalent conductivities.

Trispropylenediaminocobalt(III) *sulphate.* 11·6 Ml. of specially pure B.D.H. propylenediamine were diluted to 41 ml. with water, and poured into 17 ml. of water containing 5·3 g. of cobalt sulphate. Air was bubbled through vigorously for 5 hours. The solution was evaporated to 15 ml., and the salt precipitated by addition of 4 ml. of concentrated sulphuric acid and 40 ml. of ethyl alcohol. After cooling, the salt was filtered off. Initially, it formed an oil, but crystallised out after vigorous stirring. Methyl alcohol was used during the recrystallisations, and it caused the salt to settle out as a fine yellow powder. After several recrystallisations from water and alcohol, the salt was dried in a vacuum oven at 30—50° for 2 days. The concentrations of the stock solutions were found gravimetrically as sulphate, duplicates agreeing to within ±0·03%. The pH of the strongest solution was 4·9, and solvent corrections were applied as in the previous case.

The results are given in Table I.

Discussion.

From the conductivities of the chlorides, the limiting mobilities of the cations may be obtained with a high degree of accuracy. For this purpose Onsager's method of extrapolation

Fig. 1.

Onsager extrapolations for Λ°: (*a*) $Co(NH_3)_6Cl_3$; (*b*) $Co\ en_3\ Cl_3$; (*c*) $Co\ pn_3\ Cl_3$.

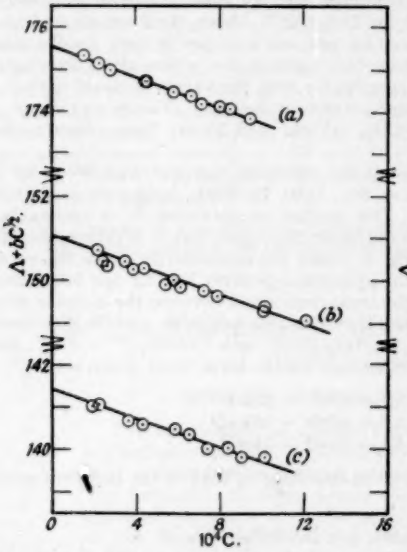
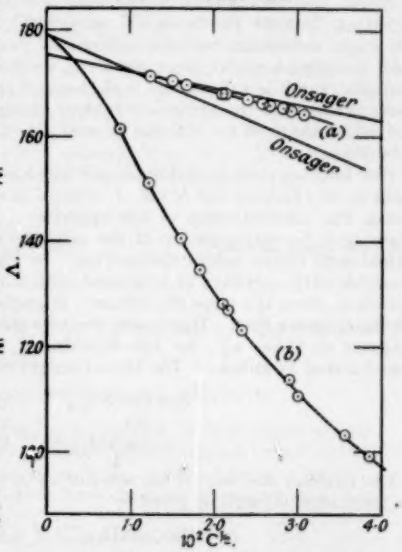


Fig. 2.

Conductivities of (*a*) $Co(NH_3)_6Cl_3$; (*b*) $[Co(NH_3)_6]_2(SO_4)_3$.



was used (*Physikal. Z.*, 1927, **28**, 277). An approximate value of Λ°, the equivalent conductivity at zero concentration, is obtained in the usual manner, *i.e.*, by plotting Λ against $C^{\frac{1}{2}}$. From this the theoretical slope b is calculated by means of Onsager's conductivity equation, and then $\Lambda + bC^{\frac{1}{2}}$ is plotted against C. These sensitive plots are shown in Fig. 1, and $\Lambda_4°$, the limiting mobilities of the cations thereby obtained, are listed in Table II. The experimental conductivity curves, Λ being plotted against $C^{\frac{1}{2}}$, lie slightly below the theoretical line; this is illustrated in the case of hexamminocobalt(III) chloride in Fig. 2. This slight difference may be attributed to ion-pair formation between the cation and chloride ions. The dissociation constant corresponding to the equilibrium $Co(NH_3)_6^{+++} + Cl' \rightleftharpoons Co(NH_3)_6Cl^{++}$ has been calculated as follows. Let $(1 - \alpha)m$ represent the concentration of $Co(NH_3)_6Cl^{++}$ ions when the total molar concentration of salt is m. The concentration of $Co(NH_3)_6^{+++}$ is then αm, and the solution is treated as a mixture of (i) the 1 : 3-valent salt $[Co(NH_3)_6^{+++}, 3Cl']$ of molar concentration αm, for which the Onsager equation is $\Lambda_{31} = 175{\cdot}55 - 221{\cdot}5I^{\frac{1}{2}}$, where I is the actual ionic strength $= \frac{1}{2}\{[Cl'] + 4[Co(NH_3)_6Cl^{++}] + 9[Co(NH_3)_6^{+++}]\} = (1 + \alpha)C$, where C is the

equivalent concentration, and (ii) the 1 : 2-valent salt $[Co(NH_3)_6Cl^{\cdot\cdot},2Cl']$ of molar concentration $(1 - \alpha)m$, for which the Onsager equation is $\Lambda_{21} = 142{\cdot}5 - 146{\cdot}5I^{\frac{1}{2}}$. In this case, the mobility of the bivalent ion-pair is taken as two-thirds of that of the tervalent cation. The solvent-corrected specific conductivity of the solution is given by

$$\begin{aligned} 10^3\kappa &= 3\alpha m\Lambda_{Co(NH_3)_6^{\cdot\cdot\cdot}} + 2(1 - \alpha)m\Lambda_{Co(NH_3)_6Cl^{\cdot\cdot}} + (2 + \alpha)m\Lambda_{Cl'} \\ &= 3\alpha m\Lambda_{31} + 2(1 - \alpha)m\Lambda_{21} \end{aligned}$$

Whence

$$\begin{aligned} \Lambda = 10^3\kappa/3m &= \alpha\Lambda_{31} + \tfrac{2}{3}(1 - \alpha)\Lambda_{21} \\ &= 94{\cdot}94 - 97{\cdot}7I^{\frac{1}{2}} + \alpha(80{\cdot}6 - 123{\cdot}8I^{\frac{1}{2}}) \end{aligned}$$

At first, α is assumed to be unity and the corresponding value of I is used in this equation, thereby giving a truer value to α with which to calculate a truer value of I, and so on, until constant figures are obtained. The dissociation constant results

$$K = \frac{\{Cl'\}\{Co(NH_3)_6^{\cdot\cdot\cdot}\}}{\{Co(NH_3)_6Cl^{\cdot\cdot}\}} = \frac{(2 + \alpha)\alpha mf_1f_2}{(1 - \alpha)f_3}$$

are given in Table I (i). The activity coefficients f_1, f_2, and f_3 have been calculated from the Debye–Huckel equation, $-\log f_i = 0{\cdot}509z_i^2I^{\frac{1}{2}}$ where z_i is the ion valency. Exactly the same treatment has been applied to the other two chlorides, and the average results are 0·032 for $Co(NH_3)_6Cl^{\cdot\cdot}$, 0·019 for Co en$_3$ $Cl^{\cdot\cdot}$, and 0·025 for Co pn$_3$ $Cl^{\cdot\cdot}$. Since these are dependent on very slight differences between theory and practice, and are sensitive to very small changes in Λ°, we cannot expect these figures to do more than indicate the orders of the dissociation constants, but it is noteworthy that they are comparable with the values obtained with 1 : 3-valent salts where the anion is tervalent, namely, 0·068 for NaP_3O_9'' (Davies and Monk, *J.*, 1949, 413), and 0·06 for $KFe(CN)_6''$ and $KCo(CN)_6''$ (James and Monk, *Trans. Faraday Soc.*, in the press).

The limiting cation mobilities obtained from the chlorides, together with 80·00 for the sulphate ion (Jenkins and Monk, *J. Amer. Chem. Soc.*, 1950, **72**, 2695), have been used in discussing the conductivities of the sulphates. This method of obtaining Λ° is preferable to obtaining it by extrapolation of the sulphate conductivities, since this is a rather uncertain method with higher-valent electrolytes. In Fig. 2, where the conductivity curve for hexamminocobalt(III) sulphate is compared with the theoretical Onsager line for the fully ionised electrolyte, there is a large discrepancy, through strong association between the complex cation and the sulphate ions. This is also the case with the other two sulphates, and the dissociation constants of these, *e.g.*, for the equilibrium $Co(NH_3)_6(SO_4)^{\cdot} \rightleftharpoons Co(NH_3)_6^{\cdot\cdot\cdot} + SO_4''$, have been obtained as follows. The three Onsager equations for the three types of ion are

$$\begin{aligned} &\text{For } Co(NH_3)_6^{\cdot\cdot\cdot} && \Lambda_1^i = 99{\cdot}2 - 224{\cdot}4I^{\frac{1}{2}} \\ &\quad ,, \ SO_4'' && \Lambda_2^i = 80{\cdot}00 - 168{\cdot}4I^{\frac{1}{2}} \\ &\quad ,, \ Co(NH_3)(SO_4)^{\cdot} && \Lambda_3^i = 33{\cdot}07 - 74{\cdot}8I^{\frac{1}{2}} \end{aligned}$$

The limiting mobility of the ion-pair is taken as one-third of that of the tervalent cation. The total ionic strength is given by

$$I = \tfrac{1}{2}\{9[Co(NH_3)_6^{\cdot\cdot\cdot}] + 4[SO_4''] + [Co(NH_3)_6(SO_4)^{\cdot}]\}$$

and if we let x be the concentration of the ion-pair at a total molar concentration m, then $I = 15m - 6x = 2{\cdot}5C - 6x$. The observed conductivity, Λ, is related to the calculated conductivity by

$$6\Lambda m = 3(2m - x)\Lambda_1^i + 2(3m - x)\Lambda_2^i + x\Lambda_3^i$$

i.e.,

$$\Lambda_1^i + \Lambda_2^i - \Lambda = (x/C)(3\Lambda_1^i + 2\Lambda_2^i + \Lambda_3^i)$$

From this, and from the ionic-strength relation, by approximating until constant x and I values are derived, the dissociation constant

$$K = \frac{\{Co(NH_3)_6^{\cdot\cdot\cdot}\}\{SO_4''\}}{\{Co(NH_3)_6(SO_4)^{\cdot}\}} = \frac{(2m - x)(3m - x)f_1f_2}{xf_3}$$

has been obtained; the activity coefficients were calculated as in the previous case. The results are given in the tables, and the average values are: $Co(NH_3)_6(SO_4)^{\cdot} = 2{\cdot}77 \times 10^{-4}$, Co en$_3$ $(SO_4)^{\cdot} = 3{\cdot}55 \times 10^{-4}$, and Co pn$_3$ $(SO_4)^{\cdot} = 1{\cdot}75 \times 10^{-4}$. The trend in these as the

size of the cobalt cation increases is in the expected direction. $LaSO_4^+$, where we have a similar type of association, has a dissociation constant of the same order as these, namely $2{\cdot}4 \times 10^{-4}$ (Jenkins and Monk, *loc. cit.*).

In Table II, the variation in the limiting mobilities of the complex cobaltic cations also follows the expected trend; *i.e.*, as the size increases, the mobility becomes less. Inserting these results in equation (2), we obtain the ionic radii *a* given in Table II. By applying the same treatment to the data for the chloride ion (Harned and Owen, *loc. cit.*) and sulphate, the radii of the anions are obtained also. Addition of these cation and sulphate ionic radii gives the size of the ion pair, which may be compared with those derived from Bjerrum's equation (1).

TABLE II.

Ion.	Λ_0°.	*a* (A.).	Ion-pair.	Radii of ion-pairs (A.). Eqn. (1).	Eqn. (2).
$Co(NH_3)_6^{+++}$	99·2	2·77	$Co(NH_3)_6(SO_4)^+$	2·56	5·06
$Co(en)_3^{+++}$	74·7	3·68	$Co(en)_3(SO_4)^+$	4·28	5·97
$Co(pn)_3^{+++}$	65·06	4·23	$Co(pn)_3(SO_4)^+$	5·76	6·52
Cl'	76·34	1·20	—	—	—
SO_4''	80·00	2·29	—	—	—

Although the sizes of the ion pairs are of the right order, it is only in the last case that the two methods give comparable results. Even with the use of Stokes's law, however, which gives the larger radii, it is probable that the calculated radii are on the small side, since the radius of the unhydrated chloride ion is 1·81 A. (Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, New York, 1939, Chap. 10) whereas our calculations for the hydrated ion give 1·20 A. It is possible that with cases where both ions forming the ion-pair are large and symmetrical, truer results might be obtained. A pointer in this direction is provided by the case of lanthanum ferricyanide (Davies and James, *Proc. Roy. Soc.*, 1948, *A*, **195**, 116), which has a dissociation constant of $1{\cdot}83 \times 10^{-4}$ at 25°, corresponding to a "Bjerrum distance" of 7·20 A. From the mobilities of the lanthanum and ferricyanide ions (Harned and Owen, *loc. cit.*), Stokes's law gives 6·67 A.

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[*Received, August 3rd*, 1950.]

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16. *An Acid-catalysed Chlorination by means of Hypochlorous Acid.*

By D. H. DERBYSHIRE and WILLIAM A. WATERS.

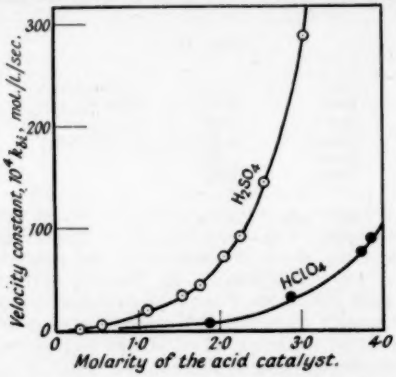
The chlorination of sodium toluene-ω-sulphonate by hypochlorous acid has been studied, both sulphuric and perchloric acids being used as catalysts. It is a second-order reaction involving chlorine cations, Cl^+ or $(H_2OCl)^+$. The formation of these active cations from hypochlorous acid becomes significant only at much higher acidities than those needed for the production of the corresponding cations from hypobromous acid (*J.*, 1950, 564). Sulphuric acid proves to be a much more effective catalyst than perchloric acid in the concentration range 0·3—4 molar.

WE have now extended our kinetic study of the acid catalysis of the bromination of sodium toluene-ω-sulphonate by means of hypobromous acid (*J.*, 1950, 564) to the analogous case of its chlorination by means of hypochlorous acid. The two substitution processes are similar in that (*a*) they are both bimolecular and (*b*) they do not proceed in the absence of a mineral acid catalyst. However, whilst the production of a bromine cation [$H^+ + HOBr \rightleftharpoons (H_2OBr)^+$] occurs so easily that a second-order velocity constant of 10^{-2} mole/l./sec. can be attained by the use of perchloric acid of only $6{\cdot}3 \times 10^{-4}$ molar concentration, a similar chlorination velocity requires the presence of 3·9M-perchloric acid, or 2·3M-sulphuric acid at the same temperature (21·5°). Consequently our measurement of an aromatic-substitution reaction involving chlorine cations has needed acid catalysts which are so concentrated that the activities of the reacting entities do not correspond closely to their molar concentrations.

The figure, which illustrates our results, shows that the chlorination of sodium toluene-ω-

sulphonate is inappreciable at hydrogen-ion concentrations of less than 0·1 mol./l. and that, as would be expected, it rises sharply in the acid-concentration range 0·5—4 molar. Consequently, *either* the chlorine cations involved, Cl^+ or $(H_2OCl)^+$, are much less active substituting agents than are the corresponding bromine cations, Br^+ or $(H_2OBr)^+$, *or*, more probably, the basic dissociation constant of hypochlorous acid, $K_b = [H_2OCl^+]/[H^+].[HOCl]$, is of the order of 10^{-4} or less than that of hypobromous acid (cf. Gonda-Hunwald, Gráf, and Körösy, *Nature*, 1950, **166**, 68; *Magyar Kémiai Folyóirat*, 1950, **56**, 204).

Acid catalysis of the chlorination of sodium toluene-ω-sulphonate by hypochlorous acid.



Whilst our observations with hypobromous acid showed that, in the concentration range of 0·1—1 molar, perchloric acid was, mole for mole, a slightly more effective catalyst than sulphuric acid, our present results show that, with respect to hypochlorous acid, sulphuric acid is the much more effective catalyst. This five- to ten-fold difference in the catalytic powers of sulphuric and perchloric acids indicates that the production of an active chlorinating agent from hypochlorous acid cannot simply be related to the molar concentrations of the ions and molecules involved in the equilibria:

$$(H_3O)^+ + HOCl \rightleftharpoons H_2O + (H_2OCl)^+ \rightleftharpoons H_2O + Cl^+$$

over the concentration range which we have found it necessary to choose.

De La Mare, Hughes, and Vernon (*Research*, 1950, **3**, 192, 242) have stated that with very reactive organic substrates, such as anisole or phenol, the rate of this acid-catalysed chlorination becomes of first order with respect to the hypochlorous acid, and of zeroth order with respect to the aromatic substrate. Consequently in their experiments the speed of formation of the cationic chlorinating agent, which they take to be the free ion Cl^+, is rate-determining. With sodium toluene-ω-sulphonate as the substrate the velocity of chlorination is unmeasurably slow in the catalyst concentrations that De La Mare, Hughes, and Vernon have used; it attains a comparable speed only in mineral acid of about twenty times those concentrations. Since this slower chlorination of sodium toluene-ω-sulphonate by hypochlorous acid is a reaction of first order with respect to the aromatic compound, our results are self-consistent with those for its catalysed bromination by hypobromous acid, and indicate that the active cationic halogenating agent has attained its equilibrium concentration with respect to the acid catalyst by way of reversible reactions which are decidedly more rapid than the aromatic substitution process. Consequently our work, by itself, does not indicate whether the active product formed from hypochlorous acid is the free, physically solvated chlorine cation, Cl^+, or the conjugate acid $(H_2OCl)^+$, or even an acyl hypochlorite, *e.g.* $Cl{\cdot}SO_4H$, but since we have worked at much higher acidities than have De La Mare, Hughes, and Vernon it is inconceivable that our reactant can have been less active than theirs.

Thermodynamic calculations (R. P. Bell and E. Gelles, forthcoming publication) show that the process

$$(H_3O)^+ + HOCl \longrightarrow (H_2OCl)^+ + H_2O$$

must be markedly endothermic, and so we hesitate, as yet, to believe that this proton transfer cannot, in some circumstances, be sufficiently slow to become rate-determining.

Experimental.

Hypochlorous Acid.—Aqueous solutions of hypochlorous acid were prepared by shaking *ca.* 0·04M-chlorine water with freshly prepared silver phosphate until the odour of free chlorine had disappeared (Shilov and Kaniaev, *J. Phys. Chem. U.S.S.R.*, 1934, **5**, 655), and then distilling the product under reduced pressure from a water-bath at 40—50°, a blackened all-glass apparatus being used (compare *J.*, 1950, 571). The hypochlorous acid solutions thus obtained were about 0·02—0·03M. and had a faintly acid reaction (pH *ca.* 4·6; glass electrode). With this method of preparation the only likely impurity is that arising from the volatilization of free chlorine. Since the hydrolysis constant of chlorine at 25° is $4·48 \times 10^{-4}$ (Jakowkin, *Z. phys. Chem.*, 1899, **29**, 655) any trace of chlorine will be completely hydrolysed to give equivalent amounts of hydrogen and chloride ions. Consequently, since hypochlorous acid itself is an extremely weak acid, the chloride contents of our preparations could be estimated from their pHs. A typical sample gave on analysis: HOCl, $3·15 \times 10^{-2}$M.; H^+, $2·6 \times 10^{-2}$M.; hence $[Cl^-]/[HOCl] = 0·07\%$. As shown below this trace of chloride would have a negligible effect upon the reaction velocity. Nevertheless the solutions of hypochlorous acid were further purified before use by shaking them with yellow mercuric oxide and then centrifuging them (compare Pryde and Soper, *J.*, 1931, 1513). As in our previous work (*loc. cit.*) the reactions were carried out with 50-ml. batches of mixtures contained in blackened glass-stoppered flasks immersed in a thermostat at 21·5° ± 0·05°. 5-Ml. samples were withdrawn at intervals for semi-microtitration, 0·01N-sodium thiosulphate being used. The comparative results of Table I show that the reaction is kinetically of second order, *i.e.*

$$d[HOCl]/dt = k_{bi}[HOCl][PhCH_2{\cdot}SO_3Na]$$

Table I.

Test of second-order reaction, sulphuric acid being used as catalyst.

$PhCH_2{\cdot}SO_3Na = 3·342 \times 10^{-2}$M.
HOCl $= 3·819 \times 10^{-3}$M.
$H_2SO_4 = 1·185$M.

Time, min.	Time, sec.	Titre, ml.	HOCl remaining, %.	10^3k_{bi}. (obs.) (mol./l./sec.).
0	0	3·74	100	—
29	58	3·35	89·6	1·85
60	0	3·00	80·2	1·86
94	54	2·68	71·7	1·78
150	0	2·21	59·1	1·80
210	0	1·79	52·1	1·81
270	0	1·45	38·8	1·83
330	0	1·17	31·3	1·84

Mean $k_{bi.} = (1·82 \pm 0·04) \times 10^{-3}$ mole/l./sec.

$PhCH_2{\cdot}SO_3Na = 6·684 \times 10^{-2}$M.
HOCl $= 3·716 \times 10^{-3}$M.
$H_2SO_4 = 1·185$M.

Time, min.	Time, sec.	Titre, ml.	HOCl remaining, %.	10^3k_{bi}. (obs.) (mol./l./sec.).
0	0	3·64	100	—
15	4	3·25	89·6	1·88
30	2	2·90	79·9	1·89
59	57	2·34	64·5	1·92
90	0	1·88	48·5	1·89
120	0	1·50	41·4	1·83
155	0	1·15	31·7	1·89
224	0	0·67	18·5	1·94

Mean $k_{bi.} = (1·89 \pm 0·05) \times 10^{-3}$ mole/l./sec.

Table II.

Chlorination of sodium toluene-ω-sulphonate with hypochlorous acid in 2·254M-sulphuric acid: the effect of the addition of chloride.

$PhCH_2{\cdot}SO_3Na$, M. $\times 10^{-2}$.	HOCl, M. $\times 10^{-3}$.	KCl, M. $\times 10^{-4}$.	$10^3k_{bi.}$ (obs.) (mol./l./sec.).
3·342	3·806	nil	9·14 ± 0·34
1·114	4·016	nil	9·18 ± 0·27
3·342	4·132	0·96	12·1 ± 1·7
3·342	4·248	3·86	20·1 ± 2·8
1·114	4·196	5·78	26·1 ± 4·2
3·342	4·280	5·78	25·9 ± 4·8

Table I indicates that the reaction rate increases very slightly when most of the hypochlorous acid has been consumed, and this trend was noticed generally. It is possibly due to the presence of a trace of chloride ions in the initial reaction mixture. Table II shows the magnitude of the reaction-velocity changes which can be brought about by adding appreciable quantities of chloride anions, so as to replace some of the hypochlorous acid by free chlorine. Though this addition does lead to an increase in the reaction velocity, and to a more noticeable divergence with reaction time from a strictly second-order course, it will be seen that as much as 8 per cent. of chloride ions has to be added to hypochlorous acid in 2·254M-sulphuric acid in order to double the velocity of chlorination of the aromatic substrate.

The data of Table I are typical of the collected results shown graphically on the figure.

One of us (D. H. D.) thanks the Department of Scientific and Industrial Research for a Maintenance Grant.

The Dyson Perrins Laboratory, Oxford. [*Received, September 9th*, 1950.]

17. *Condensation Products of Phenols and Ketones Part VI. Proof of the Flavan Structure of the Dimeride of* 4-iso*Propenyl*-m-*cresol.*

By Wilson Baker, R. F. Curtis, and J. F. W. McOmie.

The dimeride of 4-*iso*propenyl-*m*-cresol, readily prepared from *m*-cresol and acetone, is proved to be 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (II). Structure (II) has been established by a synthesis of the acid (III) obtained by oxidative degradation of the dimeride. The synthesis started from *m*-cresol or its methyl ether and ββ-dimethylacrylic acid, and proceeded *via* β-(2-methoxy-4-methylphenyl)*iso*valeric acid (V), the methyl ketone (XII), and the derived cyanohydrin.

4-*iso*Propenyl-*m*-cresol (I) readily undergoes dimerisation to yield a product, the descriptions of which are somewhat conflicting. The monomer (I) was first prepared by Fries and Fickewirth by heating 2-hydroxy-4 : β-dimethylcinnamic acid (*Ber.*, 1908, **41**, 371), and was found to yield the dimeride on long standing, or more quickly when heated with aqueous hydrochloric acid. It was stated that the dimeride could be distilled under diminished pressure and, although itself a non-crystalline resin at ordinary temperatures, it yielded a well-crystalline adduct with one molecule of diethyl ether; the adduct lost ether on exposure to the air or more quickly in a vacuum, leaving a white powder, m. p. 72—74°, but the melt would not crystallise even when seeded, presumably with the powder. These authors also obtained the same product from 4 : 7-dimethylcoumarin by treatment with zinc dust and alkali to give a hydroxythymol, followed by condensation in presence of acid (*Annalen*, 1908, **362**, 42), and it was shown later (Fries, Gross-Selbeck, and Wicke, *ibid.*, 1914, **402**, 309) that, contrary to earlier statements, the dimeride showed very weak phenolic properties.

The preparation of the same compound in a more direct manner from *m*-cresol, acetone, and hydrogen chloride is described in a number of patents taken out by Schering-Kahlbaum A.-G. (B.P. 273,684, 279856/1927; F.P. 636,119/1927; Swiss P. 127,522/1927; U.S.P. 1,696,769/1927), and the similar preparation recorded by Baker and Besly (*J.*, 1940, 1105), which gives a 40% yield, is based on B.P. 273,684. The modification given in U.S.P. 2,418,458–9/1947 (E.I. du Pont de Nemours and Co.; *Chem. Abs.*, 1947, **41**, 3918) is the most convenient and readily gives the dimeride in a yield of over 50%. The descriptions of the compound recorded in these references are essentially in agreement with the earlier work, but in B.P. 273,684, F.P. 636,119, and in Swiss P. 127,522, the acetyl derivative is stated to melt at 122—123°, whereas Baker and Besly (*loc. cit.*) showed that the m. p. is 108°, and in U.S.P. 2,418,458–9 it is stated to be 100—102°. It is thus possible that the acetyl derivative may be dimorphic, but we have been unable to obtain the higher-melting form. In Swiss P. 127,522 is the only previously recorded claim to have obtained the free dimeride in the crystalline form; it was stated to crystallise from light petroleum and had m. p. 82—83°.

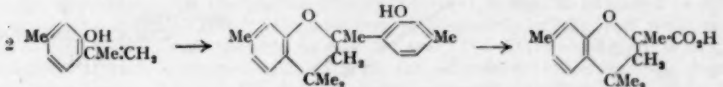
Niederl, Smith, and McGreal (*J. Amer. Chem. Soc.*, 1931, **53**, 3393) reported the preparation of the same dimeride of (I) by condensation of *m*-cresol with allyl alcohol in presence of concentrated sulphuric acid, but although the product formed with diethyl ether an adduct, m. p. 72—74°, it dissolved in aqueous potassium hydroxide and gave a dark green colour with aqueous ferric chloride, and is clearly not identical with the true dimeride, which exhibits neither of these properties. There is also doubt about the nature of the product, claimed to be the dimeride of (I), obtained by Smith and Niederl (*ibid.*, 1933, **55**, 4151) from *m*-cresol, allyl chloride, and sulphuric acid, which was stated to have m. p. 74° after crystallisation (solvent not recorded).

The dimeride of 4-*iso*propenyl-*m*-cresol has now been obtained in a beautifully crystalline state, and the isolated claim in Swiss P. 127,522 is thus substantiated. Earlier workers must, unknowingly, have handled this compound in a microcrystalline form, since it had been observed that the ether adduct, when exposed to the air, slowly lost the solvent and became a powder. This stable, free-flowing powder is, in fact, microcrystalline, and readily induces crystallisation of a solution of the dimeride in light petroleum. In comparison, the powdered non-crystalline dimeride very soon sets to a resinous mass which, although brittle, flows extremely slowly at room temperature. These physical properties of the non-crystalline dimeride are of interest and importance in connection with the study of the properties of matter which is intermediate in state between a glass and a liquid. Its advantages over other products of comparable physical properties are that it is a chemically homogeneous substance readily

prepared in quantity in a state of complete purity, and that it has a very convenient temperature range for the transition from a brittle resin to a liquid. It also exhibits strain birefringence, which at room temperature disappears in a few seconds but becomes more lasting with diminished temperature. The physical properties of this compound are under investigation at the Butterwick Research Laboratories of Imperial Chemical Industries Limited, Welwyn, Herts.

The structure of this dimeride of 4-*iso*propenyl-*m*-cresol and of related compounds has been the subject of speculation, and the position was reviewed by Baker and Besly (*Nature*, 1939, **144**, 865; this series, Part V, *J.*, 1940, 1103). After the known properties of the dimeride and the most probable course of the dimerisation which leads to a saturated product with one very weakly phenolic group had been taken into account, the conclusion was reached that the substance was most probably 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (II). Support for this view was found in the fact that the dimeride could be degraded by oxidation with potassium permanganate in acetone with loss of six carbon atoms, to give a carboxylic acid which resisted decarboxylation, and was therefore unlikely to possess an α-hydrogen atom. This degradation corresponded to the conversion of a 2-hydroxy-4-methylphenyl group into a carboxyl group, and the acid was formulated as 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (III).

An unambiguous synthesis of the acid (III) has now been achieved, and this synthetic acid is identical in all respects with that prepared by degradation of the dimeride. Moreover, it acts as a tertiary carboxylic acid by yielding carbon monoxide when treated with concentrated sulphuric acid, even at room temperature (see Bistrzychi and Mauron, *Ber.*, 1907, **40**, 4370).



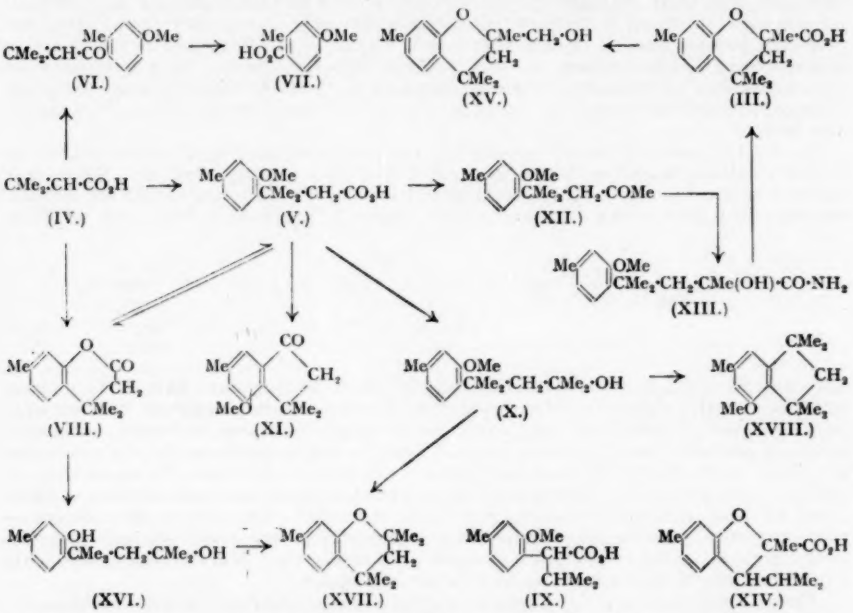
(I.) (II.) (III.)

The structure of the dimeride is thus definitely proved to be 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (II). The very simple production of a flavan in the laboratory from the *o-iso*propenylphenol (I) recalls the wide occurrence of flavan derivatives in Nature, but methyl groups in positions 2 and 4 are not commonly found in natural products, and the observation is possibly without phytochemical significance. A model of the flavan (II) shows that, by rotation of the 2-hydroxy-4-methylphenyl group, the two oxygen atoms can approach to within about 2·5 A., so the formation of a hydrogen bond is possible. This may, in part, account for the very weakly phenolic properties of the dimeride (cf. the very weakly phenolic properties of the hydroxyl group in position 5 of flavones, flavonols, etc.), but the large group in the *o*-position to the hydroxyl may also be a contributing factor.

The synthesis of the acid (III) started from ββ-dimethylacrylic acid (IV) and *m*-tolyl methyl ether, which condensed in presence of aluminium chloride to give the desired β-(2-methoxy-4-methylphenyl)*iso*valeric acid (V) in 43% yield. In addition, there was produced in smaller quantity a neutral ketone, 4-methoxy-2-methylphenyl ββ-dimethylvinyl ketone (VI), which was characterised as a 2 : 4-dinitrophenylhydrazone, and orientated by oxidation to the known 4-methoxy-2-methylbenzoic acid (VII). It was necessary to establish the structure (V) assigned to the acid, since this is a key intermediate in the synthesis. Condensation might have occurred in either of the two *ortho*-positions or in the *para*-position to the methoxyl group, and at either the α- or the β-carbon atom of the ββ-dimethylacrylic acid. That condensation had occurred *ortho* to the methoxyl group was shown by treating the acid with hydrobromic acid in acetic acid, whereupon simultaneous demethylation and lactone formation took place; methylation of the lactone (now known to be 3 : 4-dihydro-4 : 4 : 7-trimethylcoumarin, VIII) in alkaline solution with methyl sulphate regenerated the methoxy-acid (V). This lactone formation proves that the acid must be either β- (V) or α-(2-methoxy-4-methylphenyl)*iso*valeric acid (IX), or the corresponding 2-methoxy-6-methylphenyl derivatives. Attempts to prove the presence of a methylene group adjacent to the carboxyl group in either the acid or the lactone proved unexpectedly difficult, probably owing to the steric effect of the quaternary β-carbon atom; *e.g.*, no derivative of the acid could be obtained by reaction with aromatic aldehydes under the conditions of the Perkin reaction. This recalls the failure of Eijkmann to prove the presence of a methylene group in β-phenyl*iso*valeric acid (*Chem. Weekblad*, 1908, **5**, 655; for proof of structure of this acid see Hoffmann, *J. Amer. Chem. Soc.*, 1929, **51**, 2542). Again, in an attempt to apply the Barbier–Wieland degradation, the methyl ester of the acid

(V) was converted into the related tertiary alcohol [now known to be 4-(2-methoxy-4-methylphenyl)-2 : 4-dimethylpentan-2-ol (X)] by treatment with methylmagnesium iodide, but the usual degradation of *tert.*-carbinols did not occur on oxidation with chromic acid. This abnormal behaviour in an important degradative process is noteworthy, and will be described in a later communication; it is probably attributable to the quaternary β-carbon atom.

Two pieces of evidence prove that the condensation of *m*-tolyl methyl ether with ββ-dimethylacrylic acid gives the β-phenyl*iso*valeric acid (V). (*a*) Cyclodehydration of the acid with phosphoric anhydride in syrupy phosphoric acid gave a mixture containing 3 : 4-dihydro-4 : 4 : 7-trimethylcoumarin (VIII) and a ketone containing a methoxyl group, which can only be 4-methoxy-3 : 3 : 6-trimethylindan-1-one (XI); cyclodehydration could not occur either



if the acid was a derivative of α-phenyl*iso*valeric acid or if the original condensation had occurred in the alternative *o*-position to the methoxyl group. (*b*) The acid has been successfully converted *via* intermediates, now known to be (XII) and (XIII), into an acid identical with that obtained by oxidative degradation of the dimeride of 4-*iso*propenyl-*m*-cresol. If the acid possessed the structure (V) it would give ultimately the " degradation acid " (III), but if it possessed the alternative structure (IX) the acid finally synthesised would have the structure (XIV). Inspection of the carbon skeleton of the acid (XIV) shows that it could not possibly result from the degradation of any dimeride of an *iso*propenyl compound, and, therefore, structure (V) correctly represents the acid derived from *m*-tolyl methyl ether and ββ-dimethylacrylic acid. The β-addition of the aromatic nucleus to the molecule of ββ-dimethylacrylic acid is thus in line with the addition to the same acid of benzene (Eijkmann, *Chem. Weekblad*, 1908, **5**, 655; Bergmann, Taubadel, and Weiss, *Ber.*, 1931, **64**, 1493), hemimellitene, ψ-cumene, mesitylene, and *p*-xylene (Smith and Prichard, *J. Amer. Chem. Soc.*, 1940, **62**, 771), *m*-xylene (Smith and Spillane, *ibid.*, 1943, **65**, 202), 2 : 4-dimethylphenol (*idem*, *ibid.*, p. 283), and tetralin (Smith and Lo, *ibid.*, 1948, **70**, 2215), the β-addition having been established in most cases by cyclodehydration to an indanone.

The final steps in the synthesis of the acid (III) were as follows. The chloride of the acid (V) reacted with dimethylcadmium to give 4-(2-methoxy-4-methylphenyl)-4-methylpentan-2-one (XII) in 88% yield, and although this ketone readily gave a semicarbazone and a 2 : 4-dinitrophenylhydrazone it failed to give recognisable mono- or di-arylidene derivatives with

aromatic aldehydes. It likewise failed to give a derivative of *p*-nitrophenol when treated with nitromalondialdehyde and alkali (for references, see Prelog, *J.*, 1950, 426). Reaction of the ketone (XII) with anhydrous hydrogen cyanide and a trace of potassium cyanide gave a cyanohydrin which was not isolated but subjected to direct hydrolysis with concentrated hydrochloric acid in the cold, giving the hydroxy-amide, 2-hydroxy-4-(2-methoxy-4-methylphenyl)-4-methylpentane-2-carboxyamide (XIII). Finally, the amide (XIII) was boiled with aqueous hydrobromic acid in acetic acid, simultaneous hydrolysis of the amido-group, demethylation, and ring closure occurring to give the acid (III) in 41% yield.

The hydroxy-amide (XIII) is remarkable for crystallising from light petroleum (b. p. 40—60°) or pure *n*-hexane with just over one quarter of a molecule of *n*-hexane of crystallisation. In view of the chemical inertness of the aliphatic hydrocarbons, this molecular compound must be of the nature of a " clathrate," where the hydrocarbon merely occupies spaces in the crystal lattice (see Palin and Powell, *J.*, 1948, 815) and may not be present in precise stoicheiometrical proportions. The observation particularly recalls the recently investigated crystal complexes of urea with straight-chain aliphatic hydrocarbons (Schlenck, *Annalen*, 1949, **565**, 204; Zimmerscheid, Dinerstein, Weitkamp, and Marschner, *J. Amer. Chem. Soc.*, 1949, **71**, 2947), and similar complexes with thiourea (Angla, *Bull. Soc. chim.*, 1949, **16**, 12) (see also Smith, *J. Chem. Physics*, 1950, **18**, 150), and prompted us to attempt such complex formation with α-hydroxy-*iso*butyramide, $Me_2C(OH)\cdot CO\cdot NH_2$, but no evidence of the formation of crystalline adducts was obtained.

A number of other noteworthy observations have been made during the course of this work. An alternative synthesis of β-(2-methoxy-4-methylphenyl)*iso*valeric acid (V), which has practical advantages over the method already described, is first to prepare 3 : 4-dihydro-4 : 4 : 7-trimethylcoumarin (VIII) by condensation of ββ-dimethylacrylic acid with *m*-cresol, and then to methylate this as described to give the acid (V). The overall yield is 55% from ββ-dimethylacrylic acid, compared with 43% by the alternative route, and the process is simpler to carry out. The acid (V) did not undergo normal decarboxylation when heated with soda–lime. It was hoped that a much shorter synthesis of the acid (III) might be achieved by a direct preparation of the ketone (XII) from *m*-tolyl methyl ether and mesityl oxide, in view of Niederl's claim (*J. Amer. Chem. Soc.*, 1929, **51**, 2426) to have prepared 2-hydroxy-2 : 4 : 4 : 7-tetramethylchroman by condensation of *m*-cresol with mesityl oxide in presence of concentrated sulphuric acid. We found, however, that *m*-tolyl methyl ether and mesityl oxide did not condense under these conditions, and we were moreover unable to confirm Niederl's observations (cf. Smith and Prichard, *ibid.*, 1940, **62**, 771).

Unsuccessful attempts to decarboxylate the tertiary acid 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (III) by heating it either with soda–lime or with copper bronze in boiling quinoline were described in Part V of this series, but the carboxyl group was readily reduced by lithium aluminium hydride in ether, giving 2-hydroxymethyl-2 : 4 : 4 : 7-tetramethylchroman (XV). The hydroxymethyl group in (XV) could not be reduced by hydriodic acid and red phosphorus. 3 : 4-Dihydro-4 : 4 : 7-trimethylcoumarin (VIII) reacts with methylmagnesium iodide to give 2-hydroxy-4-(2-hydroxy-4-methylphenyl)-2 : 4-dimethylpentane (XVI). When treated with hydrogen chloride in methanol, (XVI) undergoes cyclodehydration to a liquid, probably 2 : 2 : 4 : 4 : 7-pentamethylchroman (XVII), characterised as a solid dibromo-derivative which is probably 6 : 8-dibromo-2 : 2 : 4 : 4 : 7-pentamethylchroman. The very slight doubt about the structure of (XVII) lies in the possibility that the tertiary carbinol group might first dehydrate to give either of two isomeric olefins, and subsequent cyclisation involving the phenolic hydroxyl group might then give rise to (XVII), or to a substituted coumaran with a five-membered ring, or to a seven-membered cyclic oxide. The last is most unlikely, and with regard to the coumaran structure the tertiary carbinol (X) is not dehydrated to an olefin by phosphoric anhydride in benzene, but gives a saturated product possessing a methoxyl group, which must therefore be either 4-methoxy-1 : 1 : 3 : 3 : 6-pentamethylindane (XVIII), or much less probably 1 : 2 : 3 : 4-tetrahydro-5-methoxy-2 : 4 : 4 : 7-tetramethylnaphthalene. Reaction of 2-hydroxy-4-(2-methoxy-4-methylphenyl)-2 : 4-dimethylpentane (X) with hydrobromic acid in acetic acid gives an alternative route to 2 : 2 : 4 : 4 : 7-pentamethylchroman (XVII), which was again characterised as the dibromo-derivative.

The properties of the acid (V) and of the related carbinol (X) are very similar to those of β-3 : 5-dimethylphenyl*iso*valeric acid and the derived dimethylcarbinol (Smith and Spillane, *loc. cit.*).

Experimental.

(M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.)

2'-Hydroxy-2 : 4 : 4 : 7 : 4'-pentamethylflavan (*Dimeric Form of* 4-iso*Propenyl*-m-*cresol*) (II).—The preparation of this compound from *m*-cresol, acetone, and hydrogen chloride was carried out either according to Baker and Besly (*loc. cit.*), or by the process recorded in U.S.P. 2,418,458–9. In either case the product was distilled under diminished pressure and further purified by crystallisation from ether–light petroleum (b. p. 40—60°) as the adduct with one molecule of diethyl ether.

The ether-free compound is readily obtained by heating the adduct on the water-bath, finally under reduced pressure, and was obtained as very large, well-developed, thick prisms from light petroleum (b. p. 40—60°) as described on p. 76. In spite of their purity, these crystals have a somewhat ill-defined m. p. of 82—84° (Found : C, 81·4; H, 7·9. Calc. for $C_{20}H_{24}O_2$: C, 81·1; H, 8·1%). At room temperature the non-crystalline dimeride crystallises extremely slowly (many months) after seeding, but the process is shortened to weeks at 35°, and is much more rapid at temperatures close to the m. p.

2 : 4 : 4 : 7-Tetramethylchroman-2-carboxylic Acid (III).—The oxidation of 2'-hydroxy-2 : 4 : 4 : 7 : 4'-pentamethylflavan (II) by potassium permanganate in acetone to give 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (III) was described by Baker and Besly (*loc. cit.*), the yield being *ca.* 8% before final purification. The oxidation has been investigated in detail, and the process now described gives this important acid in the pure state in 33% yield. Owing to the large volumes of acetone required, the oxidation can only be carried out in a single experiment on a few grams of the flavan (II). The considerable improvement in yield is due to the realisation that the degradation of the 2-hydroxy-4-methylphenyl group to a carboxyl group occurs *via* a number of intermediate carboxylic acids, and if the oxidation is carried out slowly these acids are prevented from further oxidation by being precipitated from the acetone as insoluble potassium salts. The aim has, therefore, been to oxidise (II) as rapidly as possible to the very stable acid (III), and this procedure is likely to find other useful applications. Addition of water to the acetone is not of advantage.

The flavan (II) (3 g.) was dissolved in warm acetone (30 c.c.) in a 2-l. flask, and a saturated solution of potassium permanganate in boiling acetone (900 c.c.) added rapidly. The mixture boiled spontaneously and all the permanganate was reduced in 2 minutes; the acetone was next recovered by distillation, and the residue shaken with water (100 c.c.), sodium pyrosulphite (15 g.), and 2N-hydrochloric acid (20 c.c.). The mixture was then extracted with ether (50 c.c.; 20 c.c.; 20 c.c.), the combined extracts were shaken three times with aqueous sodium carbonate, and the alkaline extracts were shaken with ethyl acetate until a colourless organic layer was obtained, then with ether, and acidified. The liberated acid rapidly solidified and was collected and dried (yield, 1·6 g.); after crystallisation from ethylene dichloride (7 c.c.) at 0° it yielded the flavan-carboxylic acid (III) (0·75 g.), m. p. 146—147°. Recrystallisation from benzene–light petroleum (b. p. 60—80°) gave a product, m. p. 148—149°, undepressed when mixed with the acid (m. p. 148—149°) prepared by Baker and Besly's method. This purified, but not the crude, acid may be recrystallised from warm, dilute methyl alcohol; it then forms small, almost rectangular tablets. The loss during crystallisation from ethylene dichloride is due to unfavourable solubility relationships, and to the presence of other acids which have not been investigated.

This acid (III) (0·1 g.), when treated with concentrated sulphuric acid (0·6 c.c.), begins to evolve carbon monoxide at 16°, and at 33° the evolution is rapid. The product, which is soluble in water and insoluble in ether, is probably a sulphonic acid.

Amide of 2 : 4 : 4 : 7-Tetramethylchroman-2-carboxylic Acid.—The acid (III) (1 g.), chloroform (10 c.c.), and thionyl chloride (1 c.c.) were refluxed for 3 hours, excess of solvent and reagent was distilled from the water-bath, and the residue shaken vigorously with concentrated aqueous ammonia and a little ether. Removal of the ether in a current of air gave the *amide* (0·93 g.), which was crystallised first from 50% methyl alcohol (35 c.c.) (charcoal) and then from light petroleum (b. p. 100—120°), and obtained as flat, square-ended prisms, m. p. 148° (Found : C, 71·8; H, 8·1; N, 5·7. $C_{14}H_{19}O_2N$ requires C, 72·1; H, 8·2; N, 6·0%).

β-(2-Methoxy-4-methylphenyl)isovaleric Acid (V).—ββ-Dimethylacrylic acid (IV) (10 g.) and *m*-tolyl methyl ether (12·2 g.) were dissolved in anhydrous benzene (25 c.c.), and to the solution powdered anhydrous aluminium chloride (16 g.) was added with vigorous stirring during ½ hour, the temperature being kept below 40°. The deep-red solution was stirred for a further 2½ hours at room temperature, and next day was poured on ice and hydrochloric acid and extracted with ether. The ethereal layer was shaken with concentrated sodium carbonate solution, separated, and worked up as described below (*A*); the alkaline layer on acidification yielded a solid acid which was collected and distilled. The fraction, b. p. 180—185°/13 mm., was crystallised from light petroleum (b. p. 40—60°), giving *β-(2-methoxy-4-methylphenyl)isovaleric acid* (V) as rhombic prisms (9·5 g., 43% yield), m. p. 93°, b. p. 183°/13 mm. (Found : C, 70·6; H, 7·9; OMe, 13·9%; equiv., 224. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1; MeO, 14·0%; equiv., 222). The yield was not improved by carrying out the reaction at −10°, as recommended by Smith and Spillane for the condensation of *m*-xylene with ββ-dimethylacrylic acid (*loc. cit.*).

Amide and p-*toluidide.* β-(2-Methoxy-4-methylphenyl)*iso*valeric acid (V) (11·5 g.) was refluxed with thionyl chloride (15 c.c.) for 20 minutes, and then distilled, giving the acid chloride as an oil, b. p. 117—118°/2 mm. (9·9 g.). The chloride (1 g.) in anhydrous ether (10 c.c.) was treated with excess of gaseous ammonia, and after ½ hour the ethereal solution was shaken with water, dried, and distilled, leaving the solid *amide* (0·65 g.), which separated from benzene–light petroleum (b. p. 60—80°) as thin plates, m. p. 111° (Found : C, 70·3; H, 8·7; N, 6·1. $C_{13}H_{19}O_2N$ requires C, 70·6; H, 8·6; N, 6·3%). The p-*toluidide* was prepared by reaction between the acid chloride (1·2 g.) and *p*-toluidine (1·1 g.) in benzene (10 c.c.) for ½ hour at room temperature. The benzene solution, after being washed with

dilute hydrochloric acid, yielded a solid which separated from benzene–light petroleum as thin needles (1·37 g.), m. p. 103° (Found: C, 76·9; H, 7·8; N, 4·7. $C_{20}H_{15}O_2N$ requires C, 77·2; H, 8·0; N, 4·5%).

4-Methoxy-2-methylphenyl β-Methylprop-1-enyl Ketone (VI).—The ethereal solution mentioned above (*A*) was washed with water, dried ($MgSO_4$), and distilled, giving *m*-tolyl methyl ether (3·2 g.; b. p. 65°/13 mm.) and the *ketone* (VI) (3·9 g., 19%), b. p. 165°/13 mm., 126—127°/0·5 mm., as a pale yellow, viscous oil (Found: C, 76·2; H, 7·5. $C_{12}H_{14}O_2$ requires C, 76·5; H, 7·8%). The preparation of the 2 : 4-*dinitrophenylhydrazone* of the ketone (VI) requires closely defined conditions. The ketone (3 drops) in dry ethanol (2 c.c.) was added to 2 : 4-dinitrophenylhydrazine (0·3 g.) in concentrated sulphuric acid (1 c.c.) and ethanol (10 c.c.), and the mixture gently warmed. The bright-red 2 : 4-dinitrophenylhydrazone slowly separated and after eight crystallisations from ethanol was obtained as dark-red, glistening needles, m. p. 156° (Found: C, 59·3; H, 5·3; N, 14·8. $C_{19}H_{20}O_5N_4$ requires C, 59·4; H, 5·2; N, 14·6%).

4-Methoxy-2-methylbenzoic Acid (VII).—To the ketone (1 g.) in acetone (20 c.c.) was added in portions at room temperature a saturated solution of potassium permanganate in acetone (*ca.* 100 c.c.). When an excess of potassium permanganate persisted for 10 minutes, the acetone was removed *in vacuo*, and the residue treated with excess of sulphur dioxide and water (20 c.c.), and then extracted with ether. The extract was shaken with aqueous sodium carbonate, and acidification of the alkaline layer yielded 4-methoxy-2-methylbenzoic acid, which, after recrystallisation from aqueous ethanol and then benzene–light petroleum (b. p. 60—80°), was obtained as fine needles (0·31 g., 38%), m. p. 175—176°, mixed m. p. with an authentic specimen, 175—176° (Found: C, 65·3; H, 6·1. Calc. for $C_9H_{10}O_3$: C, 65·1; H, 6·0%).

3 : 4-Dihydro-4 : 4 : 7-trimethylcoumarin (VIII).—β-(2-Methoxy-4-methylphenyl)*iso*valeric acid (V) (8·2 g.) was boiled under reflux for 6 hours with glacial acetic acid (50 c.c.) and aqueous hydrobromic acid (10 c.c.; *d* 1·48), and then poured into water (600 c.c.). The solution was neutralised by addition of sodium carbonate solution and cooled, and the solid 3 : 4-*dihydro*-4 : 4 : 7-*trimethylcoumarin* (6·8 g.) collected, washed, dried, and recrystallised from light petroleum (b. p. 60—80°), giving thick, almost rectangular tablets, m. p. 59·5° (5·9 g., 86%) (Found: C, 75·7; H, 7·4. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

β-(2-Methoxy-4-methylphenyl)isovaleric Acid (V) *from* 3 : 4-*Dihydro*-4 : 4 : 7-*trimethylcoumarin* (VIII).—The dihydrocoumarin (VIII) (3·8 g.) was dissolved by heating it in a solution of sodium hydroxide (20 g.) in water (50 c.c.), and then cooled; ethanol (10 c.c.) was added, and the whole treated with methyl sulphate (25·2 g.) in small portions during 10 minutes, the temperature being kept at about 50°. The solution was then heated on the water-bath for 1 hour, diluted with water (70 c.c.), and acidified with hydrochloric acid. The precipitated solid was collected after cooling to 0°, washed, dried, and recrystallised from light petroleum (b. p. 40—60°), giving rhombs (3·9 g., 88%), m. p. and mixed m. p. 93°.

4-(2-Methoxy-4-methylphenyl)-2 : 4-dimethylpentan-2-ol (X).—The acid (V) (5 g.) was converted into the methyl ester by boiling it with a saturated methanolic solution of hydrogen chloride (20 c.c.) for 4 hours. The ester, isolated in the usual way, was obtained as a colourless oil, b. p. 110—112°/0·7 mm. (5·05 g.). This ester (4·9 g.) in dry ether was added to the Grignard reagent prepared from magnesium (1·17 g.) and methyl iodide (7·1 g.) in ether (50 c.c.) in an atmosphere of nitrogen, and the mixture was refluxed for 12 hours and treated with ice and dilute hydrochloric acid. Ether-extraction yielded an oil which was boiled under reflux for 4 hours with ethanol (20 c.c.), sodium hydroxide (1 g.), and water (5 c.c.) to hydrolyse unchanged ester. Neutral material was extracted into ether, and the *pentanol* obtained as a colourless, viscous liquid, b. p. 107—109°/0·6 mm. (3·8 g.) (Found: C, 76·2; H, 10·4. $C_{15}H_{24}O_2$ requires C, 76·3; H, 10·2%).

4-Methoxy-3 : 3 : 6-trimethylindan-1-one (XI).—β-(2-Methoxy-4-methylphenyl)*iso*valeric acid (V) (6·0 g.) was finely powdered and added to a cooled mixture of phosphoric anhydride (30 g.) and syrupy phosphoric acid (30 c.c.; *d* 1·75). The mixture was heated and shaken on a steam-bath for 10 minutes, and the deep-red viscous product was poured on ice (200 g.), and the semi-solid extracted into ether (2 × 100 c.c.). The extracts were washed with 2N-sodium hydroxide (100 c.c.) (acidification gave no unchanged acid V), then with water, and dried ($MgSO_4$). Distillation of the ether left an oil, which on the addition of light petroleum (b. p. 40—60°; 5 c.c.) deposited a solid which was collected and crystallised from light petroleum (b. p. 60—80°), giving clusters of colourless, flat prisms, m. p. 230° (0·34 g.), which were not further investigated. The filtrate, after removal of the high-melting solid, gave a colourless oil, b. p. 71—100°/0·1 mm. (1·89 g.), which was boiled for 2 hours with a solution of sodium hydroxide (1·0 g.) in water (5 c.c.) and ethanol (5 c.c.), the ethanol removed under reduced pressure, and the mixture diluted and extracted with ether (2 × 50 c.c.) to remove neutral material (below). Acidification of the alkaline layer gave crude 3 : 4-dihydro-4 : 4 : 7-trimethylcoumarin (VIII), m. p. 56° (0·80 g., 15%), which after crystallisation from aqueous methanol and then from light petroleum (b. p. 40—60°) gave the characteristic, almost rectangular tablets of the pure compound, m. p. and mixed m. p. 59·5°.

The neutral ethereal extract (above) yielded an oil, and addition of light petroleum (1 c.c.) caused separation of pale yellow needles, m. p. 110° (0·156 g., 2·8%). Sublimation (100°/2 mm.) gave the *ketone* (XI) as colourless needles, m. p. 115°, both before and after crystallisation from light petroleum (Found: C, 75·8, 75·5; H, 7·6, 7·4; OMe, 15·0. $C_{12}H_{14}O_2$ requires C, 76·5; H, 7·8; OMe, 15·2%). The 2 : 4-*dinitrophenylhydrazone* separated from ethanol as fine, orange needles, m. p. 229° (Found: C, 59·4; H, 5·1; N, 14·5; OMe, 8·5. $C_{19}H_{20}O_5N_4$ requires C, 59·4; H, 5·2; N, 14·6; OMe, 8·1%).

Attempts to prepare this ketone by treatment of the acid (V) with phosphoric anhydride in boiling benzene, or by the action of stannic or aluminium chloride on the acid chloride, gave almost quantitative yields of 3 : 4-dihydro-4 : 4 : 7-trimethylcoumarin (VIII) but no ketonic material.

4-(2-Methoxy-4-methylphenyl)-4-methylpentan-2-one (XII).—This preparation was carried out in an atmosphere of nitrogen. The Grignard reagent, prepared from methyl bromide (19 g.), magnesium

(4·9 g.), and anhydrous ether (100 c.c.), was cooled to 0°, and anhydrous cadmium chloride (19·6 g.) added during 5 minutes with vigorous mechanical stirring. The mixture began to boil, and was refluxed for ½ hour on the water-bath. The ether was now rapidly removed by distillation, and dry benzene (65 c.c.) added and distilled off until 25 c.c. of distillate had collected, more benzene (120 c.c.) added, and the solution then refluxed during, and ½ hour after, the rapid addition of a solution of the chloride of β-(2-methoxy-4-methylphenyl)*iso*valeric acid (11·8 g.) in benzene (30 c.c.). After addition of ice and dilute sulphuric acid, the benzene layer was separated, the liquid extracted with ether, and the united benzene and ether extracts were dried and distilled, yielding 4-(2-*methoxy*-4-*methylphenyl*)-4-*methylpentan*-2-*one* (XII) (9·5 g., 88%) as a colourless, rather viscous liquid, b. p. 133—134°/4 mm. (Found: C, 76·3; H, 8·8. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%). This preparation must be carried out rapidly, or lower yields result. The semicarbazone separated from the usual reaction mixture at room temperature (40 hours), and was obtained from benzene–light petroleum (b. p. 40—60°) as thin plates, m. p. 138° (Found: C, 65·2; H, 8·3; N, 15·1. $C_{15}H_{23}O_2N_3$ requires C, 65·0; H, 8·3; N, 15·1%). The 2 : 4-*dinitrophenylhydrazone*, prepared by means of Brady's reagent, was precipitated after 24 hours by the addition of water and washed with dilute hydrochloric acid. It separated from alcohol as orange, microcrystalline plates, m. p. 138° (Found: C, 59·6; H, 6·0; N, 14·0. $C_{20}H_{24}O_5N_4$ requires C, 60·0; H, 6·0; N, 14·0%).

2-*Hydroxy*-4-(2-*methoxy*-4-*methylphenyl*)-4-*methylpentane*-2-*carboxyamide* (XIII).—The preceding ketone (XII) (2·2 g.) was kept for 40 hours with excess of anhydrous hydrogen cyanide (1·5 c.c.) and potassium cyanide (2 mg.). The dark mixture was then cautiously treated with concentrated hydrochloric acid (10 c.c.; saturated with hydrogen chloride at 0°) at 0°, and allowed to reach room temperature during 24 hours. After dilution with water, the mixture was extracted twice with ether, and the ethereal layer washed with dilute sodium carbonate and water, dried ($MgSO_4$), and distilled, leaving a viscous, pale brown oil. Addition of light petroleum (b. p. 60—80°) gave a solid which recrystallised from the same solvent as fine needles (0·57 g.), m. p. (rapid heating) 66—67° [the mother-liquors from the precipitation and the recrystallisation yielded unchanged ketone (XII); 1·35 g.]. The product so obtained contains *n*-hexane of crystallisation which is lost at the m. p., giving a resinous solid which may very slowly crystallise on storage and can be recrystallised from very dilute aqueous methanol as fine needles. This 2-*hydroxy*-4-(2-*methoxy*-4-*methylphenyl*)-4-*methylpentane*-2-*carboxyamide* (XIII) has m. p. 85° (Found: C, 67·9; H, 8·5; N, 5·0. $C_{15}H_{23}O_3N$ requires C, 67·9; H, 8·7; N, 5·3%). Loss of weight determinations were carried out upon the *n*-hexane *complex* by heating *in vacuo* at 80°; the complex was recovered from the resulting solid by crystallisation from pure *n*-hexane. This process was carried out repeatedly with constant loss in weight, and subsequent regeneration of the complex [Found: (*a*) C, 69·6; H, 8·9; N, 5·1; loss of weight, 7·9. (*b*) C, 69·4; H, 9·1; N, 4·9; loss of weight, 8·1. (*c*) C, 68·8; H, 9·1; loss of weight, 7·9. $C_{15}H_{23}O_3N,0{\cdot}25C_6H_{14}$ requires C, 69·1; H, 9·25; N, 4·9; loss of weight, 7·5%].

2 : 4 : 4 : 7-*Tetramethylchroman*-2-*carboxylic Acid* (III).—The amide (XIII) as the *n*-hexane complex (0·200 g.) was heated in an oil-bath at 90° for 17 hours with glacial acetic acid (2·5 c.c.) and aqueous hydrobromic acid (2·5 c.c.; *d* 1·5), then poured into water and extracted with ether. The ethereal solution yielded to aqueous sodium carbonate a solid acid (0·066 g., 41%; m. p. 142—144°), which sublimed (at 150°/360 mm.) as needles and then crystallised from aqueous methanol as the characteristic rectangular tablets of 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (III), m. p. 148—149° (Found: C, 71·6; H, 7·5. Calc. for $C_{14}H_{18}O_3$: C, 71·8; H, 7·7%). The acid prepared by oxidation of the dimeride (II) after purification by the above method had m. p. 148°, and a mixed m. p. determination of the two specimens showed no depression. The identity of the two specimens was further established by *X*-ray powder photographs kindly taken by Dr. T. Malkin. The acid is dimorphic, and at certain concentrations separates from aqueous methanol in the form of fine needles. These are unstable and change into the rectangular form when kept in the solution from which they have crystallised. The needle form appears to have the same m. p., 148—149°, as the rectangular form.

Preparation of 3 : 4-*Dihydro*-4 : 4 : 7-*trimethylcoumarin* (VIII) *from* m-*Cresol and* ββ-*Dimethylacrylic Acid*.—ββ-Dimethylacrylic acid (10·0 g., 1 mol.) was dissolved in *m*-cresol (21·6 g., 2 mols.) and treated with a rapid stream of dry hydrogen chloride for 5 minutes. Powdered aluminium chloride (28·0 g., 2·1 mols.) was then added with vigorous stirring during 15 minutes; the mixture became warm and finally very viscous, so that further stirring was impossible, after which it was kept overnight, and then heated on the steam-bath for 1 hour. The product was decomposed with ice and concentrated hydrochloric acid (50 c.c.) and extracted with ether (3 × 75 c.c.), and the extracts were shaken with 2N-sodium hydroxide (5 × 50 c.c.), dried ($MgSO_4$), and distilled, leaving an oil which rapidly crystallised on addition of light petroleum (20 c.c.; b. p. 40—60°). The colourless solid was collected (11·7 g.; m. p. 59°) and recrystallised from light petroleum (b. p. 40—60°), giving the pure 3 : 4-dihydro-4 : 4 : 7-trimethylcoumarin, m. p. and mixed m. p. with that previously described, 59·5°.

2-*Hydroxymethyl*-2 : 4 : 4 : 7-*tetramethylchroman* (XV).—Powdered lithium aluminium hydride (0·5 g.) was dissolved in sodium-dried ether (25 c.c.) with gentle warming in an atmosphere of nitrogen. A solution of 2 : 4 : 4 : 7-tetramethylchroman-2-carboxylic acid (III) (2·34 g.) in dry ether (20 c.c.) was then added dropwise during ½ hour, a vigorous reaction occurring as each drop was added. After 12 hours damp ether was added to decompose excess of reagent, then dilute hydrochloric acid, and the whole was shaken, and the ethereal layer separated, washed with dilute sodium hydroxide, then with water, dried, and distilled, leaving a colourless oil which crystallised slowly. Crystallisation from light petroleum (b. p. 40—60°) (3·5 c.c.) at 0° gave 2-*hydroxymethyl*-2 : 4 : 4 : 7-*tetramethylchroman* (XV) (1·04 g.) as large, thick, hexagonal plates which were washed with a little light petroleum at 0° and then had m. p. 47° (Found: C, 76·7; H, 8·8. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%).

4-(2-*Hydroxy*-4-*methylphenyl*)-2 : 4-*dimethylpentan*-2-*ol* (XVI).—A solution of 3 : 4-dihydro-4 : 4 : 7-trimethylcoumarin (VIII) (1·9 g.) in dry benzene (30 c.c.) was added to the Grignard reagent prepared

from methyl iodide (8·66 g.), magnesium (1·36 g.), and ether (20 c.c.) in an atmosphere of nitrogen. The ether was then removed by distillation, and the remaining mixture refluxed for 12 hours, cooled, and poured on ice and sulphuric acid (30 c.c.; 10%), and the organic layer separated; the aqueous layer was extracted with ether (100 c.c.), and the combined extracts were washed with aqueous sodium sulphite, dilute sodium carbonate, and water, dried ($MgSO_4$), and distilled. The residual oil crystallised on addition of light petroleum (20 c.c.; b. p. 40—60°), and the solid was then recrystallised from light petroleum (b. p. 60—80°), giving the *pentanol* (XVI) as fine needles (1·95 g.), m. p. 100° (Found: C, 75·7; H, 10·1. $C_{14}H_{22}O_3$ requires C, 75·7; H, 9·9%).

2 : 2 : 4 : 4 : 7-*Pentamethylchroman* (XVII).—The preceding compound (XVI) (0·75 g.) was dissolved in dry methanol (10 c.c.) and saturated with hydrogen chloride during 20 minutes, and the mixture heated for 15 minutes, and then distilled, giving a colourless oil (0·51 g.), b. p. 65—67°/0·3 mm. (Found: C, 82·2; H, 10·1. $C_{14}H_{20}O_2$ requires C, 82·3; H, 9·8%). Bromination of this **2 : 2 : 4 : 4 : 7-*pentamethylchroman*** with bromine in chloroform at 50°, the solvent being allowed to evaporate, gave a solid residue which separated from aqueous methanol in needles, m. p. 68° (Found: C, 46·3; H, 5·2; Br, 44·0. $C_{14}H_{19}OBr_3$ requires C, 46·4; H, 5·0; Br, 44·2%). This compound is undoubtedly **6 : 8-*dibromo*-2 : 2 : 4 : 4 : 7-*pentamethylchroman***.

4-*Methoxy*-1 : 1 : 3 : 3 : 6-*pentamethylindane* (XVIII).—4-(2-Methoxy-4-methylphenyl)-2 : 4-dimethylpentan-2-ol (X) (1·0 g.) in anhydrous benzene (5 c.c.) was boiled under reflux for 1 hour with phosphoric anhydride (0·2 g.). The benzene was decanted, the residue washed with benzene, and the combined solutions were washed with dilute aqueous sodium carbonate, dried, and distilled, giving **4-*methoxy*-1 : 1 : 3 : 3 : 6-*pentamethylindane*** (XVIII) as a colourless viscous oil (0·46 g.), b. p. 69—71°/0·3 mm. (Found: C, 82·7; H, 9·7; OMe, 13·9. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1; OMe, 14·2%).

Formation of* 2 : 2 : 4 : 4 : 7-*Pentamethylchroman (XVII) ***from* 4-(2-*Methoxy*-4-*methylphenyl*)-2 : 4-*dimethylpentan*-2-*ol*** (X).—The carbinol (X) (0·205 g.), hydrobromic acid (0·5 c.c.; *d* 1·48), and acetic acid (5 c.c.) were boiled for 6 hours, poured into water, and extracted with ether (2 × 5 c.c.). The extracts yielded an oil which was treated with excess of bromine in hot chloroform (5 c.c.) and evaporation in a current of air, leaving a crystalline solid. One crystallisation from methanol gave fine needles, m. p. 65° (0·205 g., 65%), raised by further crystallisation to 68°, undepressed when mixed with a specimen of the dibromo-derivative of 2 : 2 : 4 : 4 : 7-pentamethylchroman (XVII) previously described.

The authors thank Imperial Chemical Industries Limited for a grant which has met part of the expenses of this work, and for a specimen of α-hydroxy*iso*butyramide, and also Monsanto Chemicals Limited for a specimen of 4-methoxy-2-methylbenzoic acid.

THE UNIVERSITY, BRISTOL. [*Received, October 2nd,* 1950.]

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18. *Condensation Products of Phenols and Ketones. Part VII. Molecular Complexes formed by 2′-Hydroxy*-2 : 4 : 4 : 7 : 4′-*pentamethylflavan.*

By WILSON BAKER, R. F. CURTIS, and (MISS) M. G. EDWARDS.

2′-Hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (see Part VI, preceding paper) forms crystalline 1 : 1 molecular complexes with many ethers, ketones, and amines. Although salt formation may play some part in the formation of these complexes, the size and structure of the combining molecule are of importance, particularly with the ethers and ketones. The complexes with morpholine and dioxan are abnormal and contain water.

THE dimeride of 4-*iso*propenyl-*m*-cresol has been proved to be 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (formula II, Part VI). The isolation of this compound in the pure state is facilitated by the great ease with which it forms a highly crystalline complex with one molecule of diethyl ether. This complex, which has long been known (Fries and Fickewirth, *Ber.*, 1908, **41**, 371), is readily prepared by addition of ether to a light petroleum solution of the flavan, or by stirring ether into a mixture of the flavan and warm water, in which the non-crystalline flavan forms a thick oil.

In connection with other work in this laboratory on the condensation products of phenols and ketones, it was observed that the dimeride of 3-*iso*propenyl-*p*-cresol (probably 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan) yielded a mononitro-derivative which also crystallised with one molecule of diethyl ether, and it was recalled that a similar adduct was formed by the doubtless structurally related dimeride of 4-(*cyclo*hex-1-enyl)-*m*-cresol (Boettcher, Diss., Berlin, 1930). The persistence of this phenomenon in a group of related compounds suggested that the packing of the flavan molecules in the crystal was such as to leave spaces in the lattice in which a solvent molecule of suitable size could be accommodated. It was found that diethyl ketone

and diethylamine extremely readily formed very well crystallised, 1 : 1 molecular complexes with 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan, and about ten other somewhat similar substances were also found to give crystalline adducts of the same type. In an attempt to oxidise this flavan in aqueous pyridine solution it was observed that a crystalline 1 : 1 adduct was formed with pyridine, and it was then found that many aromatic and other cyclic bases formed similar adducts. The table (p. 86) sets out the compounds with which 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan forms crystalline molecular complexes.

In Part V of this series (Baker and Besly, *J.*, 1940, 1105) it was stated that the formation of the crystalline molecular complex between 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan and diethyl ether could " be used as the basis of a delicate and specific test for diethyl ether." This test is now clearly seen to be not specific for diethyl ether.

In reviewing the list of 32 substances in the table, certain generalities are apparent. A large number and variety of substances have been investigated, but only certain ethers, ketones, and aliphatic and aromatic bases yield adducts. Of the aliphatic ethers and ketones, only seven have been found to give crystal complexes; of these, diethyl ether, di*iso*propyl ether, diethyl ketone and di*iso*propyl ketone contain the grouping $CH_3 \cdot \overset{|}{C}H \cdot X \cdot \overset{|}{C}H \cdot CH_3$, where X = O or CO, methyl *n*-propyl ketone and mesityl oxide contain the grouping $CH_3 \cdot X \cdot \overset{|}{C}H \cdot \overset{|}{C} \cdot CH_3$, where X = CO, and acetylacetone is very similar in structure. It is evident that here both molecular size and chemical character are involved. Closely similar compounds which have not yet given complexes are ethyl vinyl ether, methylal, diethyl sulphide, acetone, ethyl methyl ketone, di-*n*-propyl ketone, *iso*butyl methyl ketone, di*iso*butyl ketone, *cyclo*pentanone, *cyclo*hexanone, a variety of esters with a five-atom chain, and all alcohols so far tested.

The bases which yield crystalline complexes are of a much wider variety, ranging from diethylamine and di-*n*-butylamine to quinoline and *iso*quinoline, including aniline and halogenated pyridines. The complexes are all of the 1 : 1 type, with the two exceptions mentioned below. It seems probable that salt formation is playing a prominent, though not an exclusive, part in the formation of these flavan–base complexes. Trimethylenediamine, di*iso*butylamine, mono- and di-alkylanilines, *p*-toluidine, piperidine, 2-aminopyridine, 2-iodoquinoline, and nicotine have not yielded crystalline adducts.

Two complexes only, those with dioxan and morpholine, have been found which are not of the 1 : 1 type. These particularly well crystallised products separated very slowly from light petroleum only after many days, and the explanation of this abnormal behaviour was found to be that, not only dioxan and morpholine, but also water of crystallisation was taken up. Analysis showed the presence of two molecules of the flavan, one of dioxan or morpholine, and two of water. Crystalline material could not be obtained in the absence of water. Crystallisation with two different solvents at the same time must be a very rare phenomenon. It is significant that with dioxan and morpholine, both of which are bifunctional molecules, the complex contains two molecules of the flavan to each molecule of organic solvent.

The behaviour of 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan with 2-iodopyridine requires special mention; similar behaviour has not been encountered with other adducts, but has not been deliberately sought. The 1 : 1 molecular complex was prepared by crystallisation from light petroleum in presence of excess of 2-iodopyridine. When this complex was recrystallised, *i.e.*, when it separated from a solution containing equimolecular quantities of the components, the complex had an iodine content (20·6%) corresponding to a ratio of flavan to 2-iodopyridine of approximately 1·5 : 1; and a solution containing the flavan and 2-iodopyridine in the molecular ratio of 4 : 1 deposited crystals having an iodine content (10·6%) corresponding to a ratio of approximately 3·5 : 1, respectively. No significant difference was observed between the melting points of these three specimens. This is clearly an unusual case of a molecule, the flavan, incorporating into its crystal lattice a second substance, 2-iodopyridine, in whatever proportion may be available up to a maximum of the equimolecular ratio when all the spaces in the lattice are filled. The only other comparable cases are the quinol–formic acid and quinol–acetylene complexes (Palin and Powell, *J.*, 1948, 815) in which there is incomplete filling of the spaces in the crystal lattice by organic molecules, even though the second components were present in excess; variations in the amount of the lattice filling were not recorded.

A further point of interest about these 2-iodopyridine complexes is that they are completely stable on exposure to light, whereas 2-iodopyridine, like most organic iodine compounds, becomes brown during the course of a few days. It appears that the molecules of 2-iodopyridine enclosed in the lattice are protected from oxidative attack.

X-Ray investigation of these complexes is being carried out by Dr. H. M. Powell, of the

Department of Chemical Crystallography, Oxford, and the halogen compounds listed in the table were prepared for this work. It is clear that the complexes with bases are not solely lattice compounds, but with the ethers and ketones the general form of the molecule is capable of little variation. Even here, however, it is probable that chemical or polar interaction plays a part in complex formation, since both ethers and ketones are weak proton acceptors, and salt formation or hydrogen bonding may occur between the ether or ketone on the one hand, and the phenolic hydroxyl group of the flavan on the other.

The complexes all melt with partial loss of solvent over a range of about 2°, varying from below 50° in the case of the flavan–mesityl oxide compound to over 105° in the cases of di*iso*propylamine and dioxan–water; the free crystalline flavan melts at 82—84°. The flavan–diethyl ether and flavan–diethylamine complexes have melting points some 42° above the boiling points of the solvents of crystallisation. On exposure to the air, the complexes usually begin to turn opaque within a few days, owing to loss of solvent and formation of microscopic crystals of the free flavan, though some are considerably more stable than others. Only the flavan–dioxan–water and the flavan–morpholine–water complexes are quite stable under ordinary laboratory conditions.

It is probable that 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan is unique amongst organic compounds in the great number, which could undoubtedly be increased, of substances with which it forms crystalline adducts. These adducts may find use for isolation and identification purposes and for the preparation of certain solvents in a state of very high purity.

2′-Hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan should be capable of existing in enantiomorphous forms owing to the presence of an asymmetric carbon atom in position 2. The complex with (−)-coniine was prepared in order to see if resolution could be effected, but decomposition of the apparently homogeneous, crystalline adduct gave the unchanged racemic flavan.

It may finally be mentioned that the closely related dimeride of 3-*iso*propenyl-*p*-cresol (probably 2′-hydroxy-2 : 4 : 4 : 6 : 5′-pentamethylflavan) has also been found to give molecular complexes with a large number of organic solvents, particularly bases.

Experimental.

(M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.)

2-Iodopyridine.—Considerable difficulty was experienced in attempts to repeat the preparation of 2-iodopyridine by diazotisation of 2-aminopyridine (Tschitschibabin and Rjasanzew, *J. Russ. Phys. Chem. Soc.*, 1915, **47**, 1571; see *Zentr.*, 1915, I, 1065; Craig, *J. Amer. Chem. Soc.*, 1924, **46**, 232). No reaction occurred when 2-bromopyridine was heated with a neutral solution of sodium iodide in acetone or ethyl methyl ketone (cf. preparation of 6-iodo- from 6-chloro-nicotinic acid, Klingsberg, *ibid.*, 1950, **72**, 1031), but reaction occurred in presence of acid. The method finally adopted was as follows. 2-Bromopyridine (20 g.) was boiled under reflux for 6 hours with hydriodic acid (100 c.c.; *d* 1·7), and the mixture was poured into aqueous sodium hydroxide (100 c.c.; 40%) and ice (100 g.), and extracted with ether (3 × 50 c.c.). The extracts were washed successively with water, aqueous sodium sulphite, and water, dried ($MgSO_4$), and fractionated through a 12-inch column, giving 2-bromopyridine, b. p. 75°/13 mm. (6·1 g.), and 2-iodopyridine, b. p. 93—95°/13 mm. (9·1 g., 35%) (Found : C, 29·5; H, 2·2; I, 62·3. Calc. for C_5H_4NI : C, 29·3; H, 2·0; I, 62·0%). The picrate obtained by treatment with saturated ethanolic picric acid formed thin, yellow prisms, m. p. 119—120°, from ethanol (Found : C, 30·2; H, 1·1; N, 12·4; I, 28·8. Calc. for $C_{11}H_7O_7N_4I$: C, 30·4; H, 1·6; N, 12·9; I, 29·3%).

2-Iodoquinoline.—2-Chloroquinoline (Friedländer and Ostermaier, *Ber.*, 1882, **15**, 333) (3 g.) was treated with a mixture of ethyl methyl ketone (70 c.c.) and water (1 c.c.) which had been saturated at the b. p. with sodium iodide. Hydriodic acid (1 c.c.; *d* 1·57) and water (2 c.c.) were added, and the mixture was refluxed for 30 hours. The ketone was then removed under reduced pressure, water was added and sodium hydroxide (2N.) until alkaline, and after cooling to 0° the solid was collected (3·85 g.). Recrystallisation from aqueous ethanol gave fine, very pale yellow needles, m. p. 52° (3·35 g.; 72%), raised by recrystallisation to 53° (Found : C, 42·5; H, 2·3; N, 5·5; I, 49·8. Calc. for C_9H_6NI : C, 42·4; H, 2·3; N, 5·5; I, 49·8%) (Friedländer and Weinberg, *Ber.*, 1885, **18**, 1531, give m. p. 53°).

General Method of Preparation of Complexes.—The following method has been used for the preparation of the majority of the complexes. 2′-Hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan (for preparation see Part VI) (2 g.) is dissolved in light petroleum (b. p. 40—60°) (20 c.c.), and the other component (*ca.* 1 g.) added. In many cases the complexes begin to separate almost immediately, and if the mixture is stirred the separation of fine crystals is complete in a few minutes. Large crystals are usually obtained if the mixture is not disturbed. The solid is collected, washed with a little cold light petroleum, and dried by short exposure to the air. The yields vary from about 1·5 to 2·0 g. In other cases crystalline material may only separate after one or more days, owing to lack of crystal nuclei. We have not observed the crystallisation of the free flavan from light petroleum solutions containing a solvent with which a complex is formed, but it frequently separates from such solutions containing another solvent with which complexes are not formed, particularly if the crystalline flavan itself (see Part VI) has been handled in

the laboratory. Many of the complexes may be recrystallised with some loss from light petroleum without alteration of the molecular ratio of the components.

Crystal Complexes with 2-Iodopyridine.—(*a*) The 1 : 1 *complex* was prepared from the flavan (2 g.), light petroleum (20 c.c.), and 2-iodopyridine (2 c.c.); it separated as thick prisms (2·8 g.) (for m. p. and analyses, see table). (*b*) The approximately 1·5 : 1 (flavan : 2-iodopyridine) *complex* separated, on recrystallising the 1 : 1 complex, in aggregates of very small crystals, m. p. 73—75° (Found : C, 64·6; H, 6·2; N, 2·2; I, 20·6. $1{\cdot}5C_{20}H_{24}O_2,C_5H_4NI$ requires C, 64·7; H, 6·2; N, 2·2; I, 19·6%). (*c*) The approximately 3·5 : 1 (flavan : 2-iodopyridine) *complex* separated (1·2 g.) when the flavan (2 g., 4 mols.) and 2-iodopyridine (0·35 g., 1 mol.) were mixed in light petroleum; it formed clusters of small, very thin prisms, m. p. 73—75° (Found : I, 10·6. $3{\cdot}5C_{20}H_{24}O_2,C_5H_4NI$ requires I, 10·2%). There is no evidence to suggest that the last two complexes are mixtures of the crystalline flavan and the 1 : 1 complex.

Crystalline complexes formed by 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan.

Component.	M. p. (dissociation).	Analyses : Found, % (required, %, in parentheses). Carbon.		Hydrogen.		Nitrogen.	
		1 : 1 Complexes.					
Diethyl ether	76—77°	77·8	(77·8)	9·2	(9·2)	—	
Di*iso*propyl ether	79—81	78·8	(78·4)	9·5	(9·6)	—	
Diethyl ketone	79—81	78·7	(78·5)	8·9	(8·9)	—	
Di*iso*propyl ketone	58—60	78·7	(79·0)	9·3	(9·3)	—	
Methyl *n*-propyl ketone	71—73	78·4	(78·5)	8·4	(8·9)	—	
Mesityl oxide	45—47	79·1	(79·2)	8·8	(8·6)	—	
Acetylacetone	62—64	76·0	(75·8)	8·3	(8·1)	—	
Diethylamine	97—99	78·4	(78·1)	9·4	(9·5)	3·8	(3·8)
Diethylmethylamine	75—77	78·3	(78·3)	9·7	(9·7)	3·9	(3·7)
Triethylamine	54—56	78·7	(78·6)	9·6	(9·8)	3·6	(3·5)
Di-*n*-propylamine	49—52	79·0	(78·6)	9·9	(9·8)	3·7	(3·5)
Di*iso*propylamine	105—107	78·3	(78·6)	9·8	(9·8)	3·9	(3·5)
Di-*n*-butylamine	54—56	79·2	(79·1)	10·5	(10·1)	3·2	(3·3)
Di-*sec.*-butylamine	50—52	79·0	(79·1)	9·7	(10·1)	2·8	(3·3)
*cyclo*Hexylamine	73—75	79·0	(79·0)	9·2	(9·4)	3·5	(3·5)
Benzylamine	91—93	80·5	(80·4)	8·1	(8·2)	3·7	(3·5)
Aniline	56—58	80·4	(80·2)	8·0	(8·0)	3·9	(3·6)
Pyridine	75—77	79·9	(80·0)	7·8	(7·7)	3·7	(3·7)
N-Ethylpiperidine	88—90	79·0	(79·2)	9·3	(9·5)	3·5	(3·4)
2-Methylpyridine	64—66	80·1	(80·2)	7·7	(8·0)	3·8	(3·6)
3-Methylpyridine	55—57	80·7	(80·2)	8·0	(8·0)	3·4	(3·6)
4-Methylpyridine	80—82	80·2	(80·2)	8·0	(8·0)	3·6	(3·6)
2 : 4-Dimethylpyridine	84—86	80·5	(80·4)	8·4	(8·2)	3·8	(3·5)
2 : 6-Dimethylpyridine	87—89	80·1	(80·4)	8·4	(8·2)	3·2	(3·5)
Quinoline	75—77	81·9	(81·9)	7·2	(7·3)	3·0	(3·3)
*iso*Quinoline	97—99	81·4	(81·9)	7·5	(7·3)	3·6	(3·3)
2-Methylquinoline	96—98	81·9	(82·0)	7·3	(7·5)	2·9	(3·2)
2-Bromopyridine	59—62	65·8	(66·1)	6·2	(6·2)	3·0	(3·1) *
3-Bromopyridine	50—52	66·1	(66·1)	6·2	(6·2)	3·0	(3·1) †
2-Iodopyridine	75—77	59·3	(59·9)	5·2	(5·6)	—	‡
2-Chloroquinoline	89—91	75·5	(75·7)	6·2	(6·5)	3·1	(3·1) §
(−)-Coniine	102—104	79·6	(79·4)	9·5	(9·7)	3·0	(3·3)
		Other complexes, $C_{20}H_{24}O_2 : H_2O$: Component = 2 : 2 : 1.					
Dioxan	106—108	73·6	(73·7)	8·5	(8·4)	—	‖
Morpholine	94—96	73·9	(73·8)	8·5	(8·5)	2·0	(2·0) ¶

* Found : Br, 17·5. $C_{20}H_{24}O_2,C_5H_4NBr$ requires Br, 17·6%.
† Found : Br, 17·4%.
‡ Found : I, 25·1. $C_{20}H_{24}O_2,C_5H_4NI$ requires I, 25·3%.
§ Found : Cl, 7·9. $C_{20}H_{24}O_2,C_5H_4NCl$ requires Cl, 7·7%.
‖ Loss in weight, 17·1. $2C_{20}H_{24}O_2,2H_2O,C_4H_8O_2$ requires loss, 17·3%.
¶ Loss in weight, 17·5. $2C_{20}H_{24}O_2,2H_2O,C_4H_9ON$ requires loss, 17·2%.

Complex with (−)-Coniine.—A crude, dark brown specimen of (−)-coniine (86%, 0·257 g.) was dissolved in light petroleum (b. p. 40—60°; 7 c.c.), filtered, and added to a solution of the flavan (0·888 g.) in light petroleum (10 c.c.). After treatment with charcoal, filtration, and concentration to *ca.* 7 c.c., the *complex* separated as colourless prisms [0·454 g.; m. p. *ca.* 100° (decomp.)], which, after recrystallisation from light petroleum, had m. p. 102—104° (decomp.).

Crystal Complexes with Dioxan and with Morpholine and Water.—Repeated attempts to prepare complexes in the absence of water from 2′-hydroxy-2 : 4 : 4 : 7 : 4′-pentamethylflavan and anhydrous dioxan or morpholine in light petroleum were unsuccessful. As with many other cases, complexes containing dioxan and morpholine are readily prepared in small crystals by shaking at about 50—60° a mixture of the then-fluid dimeride and water with the organic solvent.

The well-crystallised complexes were obtained as follows. The dimeride (6 g.) was dissolved in light petroleum (30 c.c.; b. p. 40—60°), and dioxan or morpholine (2 c.c.) and water (0·5 c.c.) were added, followed by enough ethyl alcohol (6 c.c.) to give a homogeneous solution. The complexes separated rapidly, preferably after seeding, in the form of large, highly refracting, rhombic crystals (yields: of dioxan–water complex, 5·7 g., collected at room temperature; of morpholine–water complex, 5·7 g., collected after final cooling to 0°). These substances give turbid solutions in warm toluene owing to the separation of water.

The authors thank Dr. W. F. Short of Boots Pure Drug Co. Ltd., Nottingham, for a gift of (−)-coniine.

THE UNIVERSITY, BRISTOL. [*Received, October 2nd*, 1950.]

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19. *An Infra-red Spectroscopic Investigation of the Reaction between Acetic Anhydride and Butyric Anhydride.*

By L. BROWN and I. F. TROTTER.

Spectroscopic evidence has been obtained for the existence of acetic butyric anhydride and the results show it to be in equilibrium with the two simple anhydrides. The equilibrium constant shows no detectable variation over the temperature range 20—100°, and consequently the heat of reaction must be very small and the equilibrium is determined by the entropy change which takes place. This must be attributed almost entirely to the change in the relative external symmetry numbers and this leads to a value of 4 for the equilibrium constant, a value giving consistent results for the extinction coefficients of the mixed anhydride. The rate of reaction is such that it can be conveniently followed spectroscopically over the temperature range 25—45°, and measurements on the velocity constant at three temperatures gave a value of about 10 kcals. for the energy of activation.

INTEREST in the mixed anhydrides was revived when in 1932 it was shown that keten would react with acetic acid to give acetic anhydride, and it was claimed that it would react with other carboxylic acids to give mixed anhydrides which were stated to be unstable to heat (Hurd and Dull, *J. Amer. Chem. Soc.*, 1932, **54**, 3427). Work on the mixed anhydrides has, however, been hampered because of the lack of any quantitative method for their analysis, an equimolecular mixture of two simple anhydrides being indistinguishable by chemical analysis from the corresponding mixed anhydride.

In an attempt to develop a spectroscopic method for the analysis of the system acetic acid–acetic anhydride–butyric acid–butyric anhydride, it was found that the spectra of mixtures of these various components varied with time. For example, if the spectrum of a mixture of acetic acid and butyric anhydride was measured immediately after preparation, it was found to be the additive sum of those of the primary constituents. If, however, the mixture was allowed to stand for some time before measurement of the spectrum, bands were observed which were characteristic of acetic anhydride and butyric acid together with certain additional bands which were not attributable to any of these four components. These additional bands were also observed in the spectra of mixtures of acetic anhydride and butyric acid and in mixtures of the two simple anhydrides, provided that in each case the solutions had been left for some time before the spectra were measured. These additional bands must be caused by formation of a mixed acetic butyric anhydride, and could in consequence be used for its detection and determination. Of these various reactions the simplest for spectroscopic study is that between the two simple anhydrides, as this gives rise to a three-component system as opposed to the five-component system obtained if a carboxylic acid is used as one of the primary components.

EXPERIMENTAL.

The samples used for the study of the reactions were the following: (*a*) Acetic anhydride obtained by treatment with sodium of a commercially pure sample, followed by fractionation from a mixture of sodium and sodium acetate; the final fraction was spectroscopically free from acetic acid. (*b*) Butyric anhydride prepared by fractionation of a commercially pure sample; the final fraction was spectroscopically free from butyric acid. (*c*) Carbon tetrachloride obtained by washing a commercial sample with sodium hydroxide solution, then with water, and drying (Na_2SO_4) and fractionating it; the product was transparent to radiation at 3 μ. in a 2-cm. absorption cell.

The spectra were measured on a Hilger D.209 spectrometer fitted with a sodium chloride prism and used as a single-beam photographic recorder.

All the spectra were measured in a sealed absorption cell, about 0·1 mm. thick, similar to that described by Colthup (*Rev. Sci. Instr.*, 1947, **18**, 64). Liquid was introduced into the cell through one of two stainless-steel tubes, and could be removed by inserting the two tubes into two pieces of pressure tubing, one connected through a drying tube to the atmosphere and the other to a vacuum line. Provision was also made for flushing the cell with a stream of carbon tetrachloride.

In making quantitative measurements, a trace was taken of the sample followed immediately by one of the solvent on the same wave-length scale. This method of superimposing the background was justified by the results obtained. The effect of scattered radiation was minimized by using a glass scatter shutter.

In following the rates of reaction, the reaction vessel was placed in a constant-temperature bath and continuously agitated by an eccentric drive taken from the stirrer motor.

Results and Discussion.

(*a*) *Choice of Characteristic Frequencies.*—The spectra of solutions of acetic anhydride and butyric anhydride in carbon tetrachloride solution are shown in Fig. 1 over the range 950—1250 cm.$^{-1}$. In Fig. 2 the broken line represents the spectrum of a mixture of the two anhydrides at the same concentrations as in Fig. 1 on the assumption that no interaction takes place, and the full line represents the observed spectrum after equilibrium is reached. Of the new bands which appear, the strongest is at 1000 cm.$^{-1}$, and its appearance is accompanied by a decrease in the intensities of the butyric anhydride and acetic anhydride bands at 1029 and 1125 cm.$^{-1}$, respectively. These three bands occur in a relatively narrow region of the spectrum

Fig. 1.

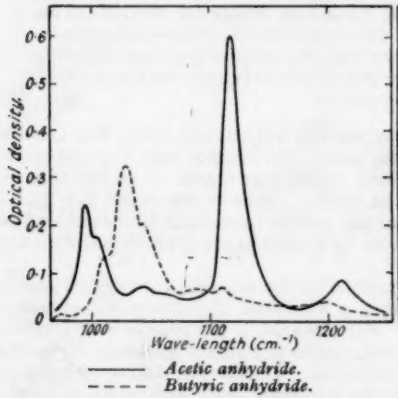
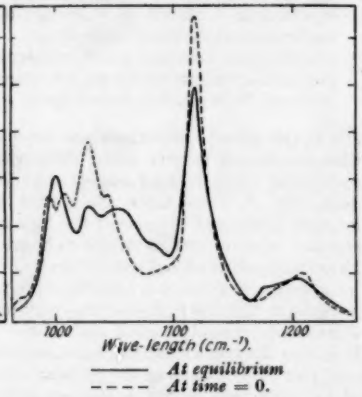


Fig. 2.

Mixture of acetic and butyric anhydrides.



which can conveniently be covered at one setting of the spectrometer slits (0·025 cm.), and moreover, carbon tetrachloride has very little absorption in this region. Thus the most convenient choice of key frequencies is as follows:

Acetic butyric anhydride	1000 cm.$^{-1}$ (ν_1)
Butyric anhydride	1029 cm.$^{-1}$ (ν_2)
Acetic anhydride	1125 cm.$^{-1}$ (ν_3)

In order to analyse mixtures of these three components, it is necessary to know the extinction coefficients of each component at each of the three key frequencies. For the two simple anhydrides this presents no difficulty, but, as from the nature of the reaction the mixed anhydride cannot be isolated, it is necessary to obtain the extinction coefficients of acetic butyric anhydride indirectly.

(*b*) *Measurement of the Extinction Coefficients of Acetic and Butyric Anhydrides at* ν_1, ν_2, *and* ν_3.—Solutions of acetic and butyric anhydrides were made up in carbon tetrachloride at a series of concentrations, and the measured optical densities at ν_1, ν_2, and ν_3 plotted against concentration. In each case straight lines were obtained which passed through the origin, showing that over the concentration range studied the solutions obeyed Beer's law, which may be written in the form $D_\nu = -\log_{10} T_\nu = \alpha_\nu cd$, where D_ν is the optical density and T_ν the transmission at frequency ν, c is the concentration of the component, d the cell thickness, and

α_ν the extinction coefficient. It is convenient to compound the cell thickness and the extinction coefficient to give ε_ν, the apparent extinction coefficient, which may be defined by the equation $D_\nu = \varepsilon_\nu f$.

The units chosen to express the concentration were g. per 50 ml. of solution. Then, if ε_{ij} is the extinction coefficient defined in this way for the ith component at the jth frequency, the results obtained for the two simple anhydrides may be summarized as follows:

$$\varepsilon_{11} = 0{\cdot}089;\ \varepsilon_{22} = 0{\cdot}660;\ \varepsilon_{33} = 0{\cdot}105;\ \varepsilon_{31} = 0{\cdot}350;\ \varepsilon_{32} = 0{\cdot}058;\ \varepsilon_{33} = 1{\cdot}363$$

As it was intended to measure the rate of the reaction at a series of temperatures, it was necessary to see if any consistent error was introduced if the solutions were measured at temperatures more than a few degrees removed from room temperatures: it was found that no such error was introduced over the temperature range used.

(*c*) *Variation of Equilibrium Constant with Temperature.*—Standard solutions of acetic and butyric anhydrides were prepared at room temperature, then brought to the appropriate temperature, mixed in various proportions, and allowed to come to equilibrium. In order to carry out measurements at 100°, the reaction was carried out in a sealed tube, and the equilibrium subsequently frozen in solid carbon dioxide–acetone. The measured mean equilibrium values of the optical density for a series of experiments are listed in Table I, each being the mean of at least six measurements. The initial concentrations of butyric anhydride, $C_2°$, and acetic anhydride, $C_3°$, are in g./50 ml.

TABLE I.

Expt.	Temp.	$C_2°$.	$C_3°$.	D_1.	D_2.	D_3.	Expt.	Temp.	$C_2°$.	$C_3°$.	D_1.	D_2.	D_3.
A	25°	0·538	0·647	0·395	0·253	0·712	D	25°	0·808	0·431	0·358	0·423	0·463
B	35	0·538	0·647	0·401	0·257	0·723	E	35	0·808	0·431	0·355	0·421	0·463
C	45	0·538	0·647	0·395	0·256	0·706	F	45	0·808	0·431	0·351	0·430	0·457
G	19·7	0·650	0·682	0·444	0·299	0·760	I	19·7	0·871	0·439	0·360	0·445	0·476
H	100	0·650	0·682	0·440	0·304	0·760	J	100	0·871	0·439	0·365	0·441	0·477

From the results it follows that within the limits of experimental error the equilibrium constant is independent of temperature over the range 20—100°, and this is evident without any knowledge of the extinction coefficients of the mixed anhydride. The thermodynamic implications of this result are that the overall heat of reaction is zero, that there is no change in internal energy, and that the equilibrium constant is determined solely by the entropy change. In this respect the reaction is evidently analogous to certain processes of ester exchange (Calingaert *et al.*, *J. Amer. Chem. Soc.*, 1939, **61**, 2748), to the redistribution of metal alkyls (*idem*, *ibid.*, p. 2755; 1940, **62**, 1104, 1107, 1542; 1941, **63**, 94), and to the redistribution of halogen that takes place between the glycol dihalides (*idem*, *ibid.*, 1940, **62**, 1545).

The change in entropy ($\Delta S°$) for this type of reaction should be measured by the relative external symmetry numbers σ of the molecules involved in the equilibrium; the only other appreciable contributions to $\Delta S°$ would lie in the effect of the redistribution of mass on the translational entropies and in the redistribution of the principal moments of inertia on the rotational entropies. These contributions are likely to be small, so that the controlling factor in the equilibrium in the case where the heat content change is zero would be expected to be $(\Delta S°)\sigma$. For the reaction in question the relative external symmetry numbers are 2 for the simple anhydrides and unity for the mixed anhydride, which leads to a value of 4 for the equilibrium constant when the concentrations are expressed in moles per unit volume.

(*d*) *Calculation of Extinction Coefficients of the Mixed Anhydride.*—It is not necessary to know the value of the equilibrium constant to evaluate the extinction coefficients of the mixed anhydride, but without this knowledge the overall accuracy of the calculation is low and the best results are obtained by using the value of the equilibrium constant derived above. Suppose C_1, C_2, and C_3 are the equilibrium concentrations of acetic butyric, butyric, and acetic anhydrides in g. per unit volume, and M_1, M_2, and M_3 are the respective molecular weights. Then,

$$C_1^2/C_2C_3 = 4M_1^2/M_2M_3 = 4{\cdot}190 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The equilibrium concentrations will be related to the initial concentrations of the two simple anhydrides by the equations

$$C_1/260 = (C_2° - C_2)/158 = (C_3° - C_3)/102$$

whence

$$C_2 = C_2° - 0{\cdot}608C_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and

$$C_2 = C_2^\circ - 0{\cdot}392C_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Substitution for C_2 and C_3 in equation (1) gives

$$C_1 = 4{\cdot}190C_2^\circ C_3^\circ/(2{\cdot}550C_3^\circ + 1{\cdot}643C_2^\circ) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Hence, by using equations (2), (3), and (4) it is possible to derive C_1, C_2, and C_3 from the initial concentrations.

The optical densities at ν_1, ν_2, and ν_3 are related to the unknown extinction coefficients by the equations

$$\left.\begin{aligned} D_1 &= \varepsilon_{11}C_1 + 0{\cdot}089C_2 + 0{\cdot}350C_3 \\ D_2 &= \varepsilon_{12}C_1 + 0{\cdot}660C_2 + 0{\cdot}058C_3 \\ D_3 &= \varepsilon_{13}C_1 + 0{\cdot}108C_2 + 1{\cdot}363C_3 \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Hence from equation (5) it is possible to evaluate ε_{11}, ε_{12}, and ε_{13} from the calculated concentrations C_1, C_2, and C_3 and from the measured equilibrium optical densities. The results of these calculations are given in Table II.

TABLE II.

Expt.	C_2°.	C_3°.	D_1.	D_2.	D_3.	ε_{11}.	ε_{12}.	ε_{13}.
I, IV, VII	0·674	0·540	0·375	0·326	0·585	0·396	0·179	0·236
II, V	0·898	0·361	0·322	0·465	0·380	0·397	0·184	0·231
III	0·448	0·695	0·395	0·208	0·808	0·405	0·181	0·240
A, B, C	0·538	0·647	0·397	0·255	0·714	0·404	0·186	0·208
D, E, F	0·808	0·431	0·355	0·425	0·461	0·411	0·206	0·243
G, H	0·650	0·682	0·442	0·302	0·760	0·411	0·172	0·239
I, J	0·871	0·439	0·362	0·443	0·476	0·400	0·174	0·255
VI	0·337	0·539	0·303	0·161	0·624	0·406	0·190	0·228
VIII	0·561	0·449	0·318	0·275	0·494	0·409	0·188	0·249
IX	0·481	0·385	0·270	0·234	0·422	0·406	0·175	0·251
					Mean	0·404	0·184	0·236

By substituting these values for the extinction coefficients in equation (5) and solving for the concentration terms, the equations

$$\left.\begin{aligned} C_1 &= 3{\cdot}106D_1 - 0{\cdot}290D_2 - 0{\cdot}785D_3 \\ C_2 &= -0{\cdot}829D_1 + 1{\cdot}618D_2 + 0{\cdot}144D_3 \\ C_3 &= -0{\cdot}500D_1 - 0{\cdot}078D_2 + 0{\cdot}865D_3 \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

are obtained, from which C_1, C_2, and C_3 may be obtained directly in terms of D_1, D_2, and D_3.

The constancy of the values of the extinction coefficients derived from the various experiments (Table II) provides confirmation of the value of the equilibrium constant deduced from the observation that the equilibrium optical densities were independent of temperature.

(*e*) *Determination of the Energy of Activation of the Reaction.*—It was found that the reaction proceeded at a conveniently measurable rate over the temperature range 25—45°. At 25° it was sufficiently slow to enable the spectrum to be measured over all three characteristic frequencies, but at 35° and 45° the time between successive measurements had to be cut to a minimum and it was found convenient to follow the reaction by measuring D_3 alone until equilibrium was reached, whereupon the optical densities at all three frequencies were measured. Thus at 25° (Runs I—III) measurements were made at intervals of 9—10 minutes, whereas at 35° and 45° the time interval was reduced to 3·5—4·5 minutes (Runs IV—IX).

For a reaction of the type $A + B \rightleftharpoons 2C$, if the initial concentrations of A, B, and C are a, b, and 0 moles per unit volume, if after time t the concentration of C is $2x$ moles per unit volume, and if the equilibrium constant is 4, then the velocity constant of the forward reaction (k) is given by the expression

$$k = \frac{-2}{t} \cdot \frac{1}{a+b} \ln\left(1 - \frac{a+b}{ab}x\right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

For the reaction between butyric and acetic anhydrides: $a = C_2^\circ/158$; $b = C_3^\circ/102$, and $2x = C_1^t/130$, whence

$$k = \frac{-1}{t} \cdot \frac{728}{C_2^\circ + 1{\cdot}549C_3^\circ} \log_{10}\left(1 - \frac{C_2^\circ + 1{\cdot}549C_3^\circ}{C_2^\circ C_3^\circ} \cdot \frac{C_1^t}{2{\cdot}55}\right) \quad . \quad . \quad . \quad (8)$$

Direct substitution in equation (8) will give k in units of 50 ml. mole^{-1} min.$^{-1}$.

If D_j° is the initial optical density at the jth frequency and D_j^t is the optical density at time t, then

$$D_j^t = \varepsilon_{1j}C_1^t + \varepsilon_{2j}C_2^t + \varepsilon_{3j}C_3^t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

Eliminating C_2^t and C_3^t by means of equations (2) and (3) and writing the change in optical density between times t and 0 as ΔD_j^t, we have

$$\Delta D_j^t = (\varepsilon_{1j} - 0{\cdot}608\varepsilon_{2j} - 0{\cdot}392\varepsilon_{3j})C_1^t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

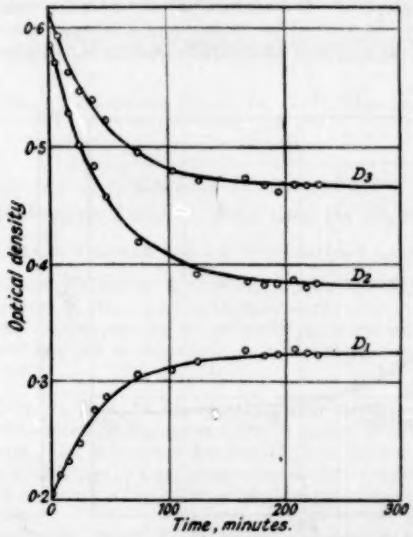
Insertion of the experimental values of the extinction coefficients in equation (10) gives

$$\Delta D_1^t = 0{\cdot}214C_1^t; \quad \Delta D_2^t = -0{\cdot}240C_1^t; \quad \Delta D_3^t = -0{\cdot}364C_1^t \quad . \quad . \quad . \quad (11)$$

From equation (11) it follows that, knowing the equilibrium values of ΔD_1, ΔD_2, and ΔD_3, it is possible to calculate any two of the optical densities at time t if the third is known. Conversely, if all three optical densities are known, it is possible to use equation (11) to average the three sets of results. This was done for runs I, II, and III, so that all three rate curves could be averaged to give a mean value for the velocity constant.

FIG. 3.

Run II. Reaction at 25°.



In Fig. 3 is shown the variation of optical density with time for the three key frequencies in run II, the reaction being measured at 25°. Runs I, IV, and VII started with the same initial concentrations but were carried out at 25°, 35°, and 45°, respectively, and the rate curves (D_3 versus t) for these runs are illustrated in Fig. 4. The velocity constants were obtained by measuring D_3 at various times from the rate curves, obtaining C_1^t from equation (11), and substituting the value so obtained together with the values of C_2° and C_3° in equation (8), the mean value of k for each curve being taken. The results obtained for the velocity constants are given in Table III.

For each set of runs at a given temperature, the mean variation in the velocity constant is about $\pm 14\%$. This could be accounted for by the errors introduced in drawing the rate curves, but there is a further source of error, namely, the possibility of absorption of a certain amount of water during the preparation of the solutions. It was found during the preliminary measurements that reactions of the following type can take place: AcOH + Ac′OAc′ $\rightleftharpoons$ AcOAc′ + Ac′OH, where Ac and Ac′ are two acyl radicals.

Reactions of this type have been known for some time, and it is thus possible that the reaction between the two anhydrides is catalysed by acid. Although the anhydrides and the carbon tetrachloride were carefully purified before use, it is difficult to obtain an anhydride completely free from acid, and as anhydrides are hygroscopic, a certain amount of water could be taken up during the preparation of the solutions and during sampling. If the amount so taken up were to vary from run to run it might introduce a variation in the velocity constant.

TABLE III.

Run.	Temp., °K.	k, 50 ml. mole^{-1} min.$^{-1}$.	k (mean), l. mole^{-1} min.$^{-1}$.
I	298	3·25	0·196
II	298	4·77	
III	298	3·71	
I, II, III	298	3·91	
IV	308	5·31	0·336
V	308	7·83	
VI	308	7·01	
IV, V, VI	308	6·72	
VII	318	10·50	0·595
VIII	318	10·90	
IX	318	14·30	
VII, VIII, IX	318	11·90	

In Fig. 5 is shown a graph of $-\ln k$ against $1/T$, and from the slope of the line the energy of activation is 10,600 cals. In view of the variation in k between one run and another and the, small temperature intervals available for study, the energy of activation may be taken as being of the order of 10 kcals.

FIG. 4.

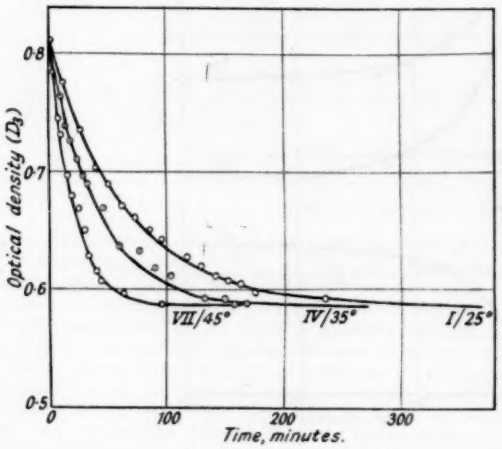
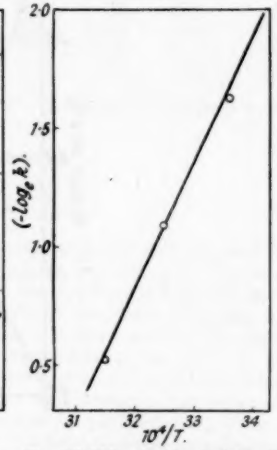


FIG. 5.



E = 10,600 *cals. (from slope of line).*

The observation that acetic butyric anhydride exists in equilibrium with the two simple anhydrides is of interest in connection with the work of Verkade (*Rec. Trav. chim.*, **1916**, **35**, 299) and of Kilpatrick and Kilpatrick (*J. Amer. Chem. Soc.*, **1930**, **52**, **1418**) on acetic propionic anhydride. They found that the hydrolysis of the mixed anhydride proceeded as a first-order reaction with a reaction velocity intermediate between the values for the symmetrical anhydrides, and interpreted this result as showing that they were dealing with a true mixed anhydride and not with a mixture of the two simple anhydrides. If the rate of disproportionation of acetic propionic anhydride is comparable with that of acetic butyric anhydride, then at the temperature at which the rate of hydrolysis was measured, 0°, the rate of disproportionation would be very slow compared with the rate of hydrolysis, so that the disproportionation reaction could be neglected.

It is noteworthy that, once the equilibrium constant for the reaction between the two anhydrides is known, the extension of the analytical method to include the components acetic acid and butyric acid is relatively simple. The characteristic frequencies chosen for butyric acid and acetic acid were 1220 cm.$^{-1}$ (ν_4) and 1288 cm.$^{-1}$ (ν_5), respectively, and the optical densities at the five key frequencies are related to the concentrations of the components by the equations

$$\begin{aligned}
D_1 &= 0{\cdot}405C_1 + 0{\cdot}089C_2 + 0{\cdot}350C_3 + 0{\cdot}021C_4 + 0{\cdot}041C_5 \\
D_2 &= 0{\cdot}184C_1 + 0{\cdot}660C_2 + 0{\cdot}058C_3 + 0{\cdot}053C_4 + 0{\cdot}034C_5 \\
D_3 &= 0{\cdot}236C_1 + 0{\cdot}108C_2 + 1{\cdot}363C_3 + 0{\cdot}021C_4 + 0{\cdot}009C_5 \\
D_4 &= 0{\cdot}093C_1 + 0{\cdot}028C_2 + 0{\cdot}171C_3 + 0{\cdot}184C_4 + 0{\cdot}026C_5 \\
D_5 &= 0{\cdot}043C_1 + 0{\cdot}043C_2 + 0{\cdot}011C_3 + 0{\cdot}195C_4 + 0{\cdot}880C_5
\end{aligned}$$

Solving for the concentration terms, we have

$$\begin{aligned}
C_1 &= +3{\cdot}099D_1 - 0{\cdot}284D_2 - 0{\cdot}776D_3 - 0{\cdot}052D_4 - 0{\cdot}124D_5 \\
C_2 &= -0{\cdot}751D_1 + 1{\cdot}606D_2 + 0{\cdot}172D_3 - 0{\cdot}378D_4 - 0{\cdot}018D_5 \\
C_3 &= -0{\cdot}464D_1 - 0{\cdot}074D_2 + 0{\cdot}861D_3 - 0{\cdot}042D_4 + 0{\cdot}017D_5 \\
C_4 &= -1{\cdot}039D_1 - 0{\cdot}024D_2 - 0{\cdot}451D_3 + 5{\cdot}732D_4 - 0{\cdot}166D_5 \\
C_5 &= +0{\cdot}121D_1 - 0{\cdot}058D_2 + 0{\cdot}119D_3 - 1{\cdot}249D_4 + 1{\cdot}169D_5
\end{aligned}$$

The results serve to show the applicability of the spectroscopic method to the study of chemical reactions, in particular to those in which no chemical analysis of the system is possible.

The authors thank Mrs. J. M. Shreeve for her assistance in the experimental work, Mr. A. W. Porter for the construction of the absorption cell, and the Directors of Courtaulds Limited for permission to publish this work.

COURTAULDS LIMITED, No. 1 LABORATORY, COVENTRY. [*Received, September 2nd*, 1950.]

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20. *Syntheses in the Naphthalene Series. Part IV.* 3-*Hydroxy*-1 : 4-*naphthaquinone*-2-*acetic Acid and its Homologues.*

By GABRA SOLIMAN and (in part) ALBERT LATIF.

Ethyl phenylacetylsuccinate and ethyl α-phenylacetylglutarate, prepared by substitution of ethyl γ-phenylacetoacetate, were converted into a γ- and a δ-lactone, respectively, by the action of sulphuric acid at 40°. The two lactones were oxidised to 3-hydroxy-1 : 4-naphthaquinone-2-acetic and -2-β-propionic acid.

IN previous communications (*J.*, 1944, **53**, 55, 56), the utility of ethyl γ-phenylacetoacetate as a synthetic reagent was illustrated by the preparation of 2-alkyl-1 : 3-dihydroxynaphthalenes, 1-hydroxy-2 : 3-benzfluorene, and 4-hydroxy-2-methyl-5 : 6-benzocoumaran. Furthermore, a new synthesis of 2-alkyl-3-hydroxy-1 : 4-naphthaquinones was described, and the object of this paper is to record the results of a brief survey of the applicability of this synthesis to the acidic members of the series.

Ethyl phenylacetylsuccinate (ethyl β-carbethoxy-γ-keto-δ-phenylvalerate) (I; R = $CH_2{\cdot}CO_2Et$) and ethyl α-phenylacetylglutarate (ethyl 4-carbethoxy-5-keto-6-phenylhexanoate) (I; R = $CH_2{\cdot}CH_2{\cdot}CO_2Et$) were prepared by the action of ethyl bromoacetate and ethyl β-iodopropionate, respectively, on ethyl sodio-γ-phenylacetoacetate in absolute alcohol. The two esters were shown to be α-substituted by hydrolysis; the former yielded β-phenylacetylpropionic acid (Fittig and Stern, *Annalen*, 1892, **268**, 89; Russwurm, Stobbe, and Schulz, *ibid.*, 1899, **308**, 179; Lukeš, *Coll. Trav. Chim. Tchecosl.*, 1932, **4**, 181; *Chem. Zentr.*, 1932, I, 3062), and the latter ester yielded γ-phenylacetylbutyric acid, characterised by the formation of a semicarbazone.

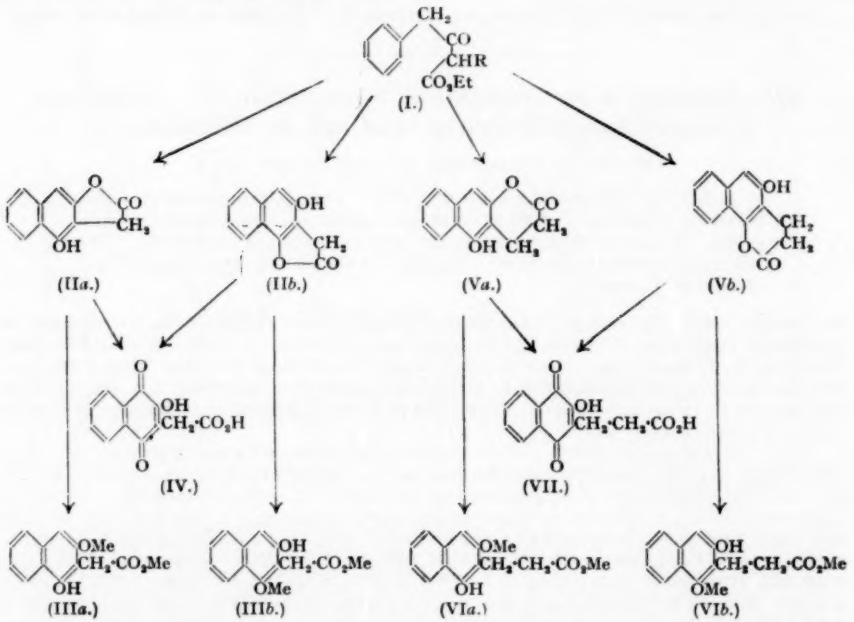
Whereas cyclisation of ethyl phenylacetylmalonate (I; R = CO_2Et) by cold sulphuric acid (cf. Metzner, *Annalen*, 1897, **298**, 383; Soliman and West, *J.*, 1944, 53) yielded 2-carbethoxy-1 : 3-dihydroxynaphthalene, cyclisation of its next two higher homologues at 40° proceeded to a secondary stage of ring closure. Ethyl phenylacetylsuccinate gave a product $C_{12}H_8O_3$ which formed a monoacetate, and yielded a methyl methoxy-ester $C_{14}H_{14}O_4$ on treatment with hydrogen chloride in methanol. Formation of this ester (III*a* or *b*) by methanolysis

indicated that this cyclisation product is a γ-lactone (II*a* or *b*) which arose by dehydration of such an intermediate as 1 : 3-dihydroxynaphthalene-2-acetic acid, and would be analogous to the conversion of 3-hydroxynaphthalene-2-acetic acid into 5 : 6-benzocoumaran-2-one by the action of heat or phosphoric oxide (Stoermer, *Annalen*, 1900, **313**, 91; Eistert and Krizkalla, *J. pr. Chem.*, 1935, **143**, 50; Eistert, *Ber.*, 1936, **69**, 1074). This conclusion is supported by the fact that the lactone was quantitatively oxidised in presence of alcoholic potassium hydroxide (cf. Soliman and Latif, *J.*, 1944, 55) to 3-hydroxy-1 : 4-naphthaquinone-2-acetic acid (IV), previously synthesised by lengthy methods (Liebermann, *Ber.*, 1900, **33**, 566; Bamberger and Praetorius, *Monatsh.*, 1911, **22**, 587; Newman, Crowder, and Anderson, *J. Biol. Chem.*, 1934, **105**, 279).

Similarly, ethyl α-phenylacetylglutarate yielded on cyclisation under identical conditions a crystalline product $C_{13}H_{10}O_3$ which formed a monoacetate and a methyl methoxy-ester $C_{15}H_{16}O_4$ (VI*a* or *b*) and was thus shown to be a δ-lactone (V*a* or *b*). Furthermore, this lactone was also quantitatively oxidised to 3-hydroxy-1 : 4-naphthaquinone-2-β-propionic acid (VII), recently prepared by peroxide alkylation of 2-hydroxy-1 : 4-naphthaquinone (Fieser *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 3206).

However, 2-carbethoxy-3-hydroxy-1 : 4-naphthaquinone, prepared by oxidation of 2-carbethoxy-1 : 3-dihydroxynaphthalene in presence of alcoholic potassium hydroxide (Soliman and Latif, *loc. cit.*), was found to possess the same properties as the product obtained by Fieser *et al.* (*loc. cit.*) by oxidation of 4-amino-2-carbethoxy-1 : 3-dihydroxynaphthalene with dichromate.

Owing to the difficulties encountered in isolating and purifying the above-mentioned lactones, they have not been fully characterised but attempts are in progress to differentiate between the alternative formulæ illustrated.



In an attempt to study the action of sulphuric acid on other derivatives of ethyl γ-phenylacetoacetate, ethyl α-diphenylmethyl-γ-phenylacetoacetate (I; R = $CHPh_2$) was prepared in the usual manner and shown to be α-substituted by hydrolysis to ββ-diphenylpropionic acid (Henderson, *J.*, 1891, **59**, 731) and benzyl 2 : 2-diphenylethyl ketone. However, by the action of sulphuric acid at room temperature or at 40° it gave a resinous product which could not be converted into a crystalline derivative.

Experimental.

(M. p.s are not corrected; microanalyses were done by Drs. Weiler and Strauss, Oxford.)

Ethyl Phenylacetylsuccinate (*Ethyl β-Carbethoxy-γ-keto-δ-phenylvalerate*).—This was prepared by the action of ethyl bromoacetate (1 mol., 16·6 g.) on ethyl sodio-γ-phenylacetoacetate (from ester, 20·6 g., and sodium, 2·3 g., in absolute alcohol). The reaction was complete after 4 hours' heating; alcohol was then distilled off, and the ester extracted with ether and distilled. The fraction (20 g.), b. p. 182—184°/3 mm., gave a violet-red colour with ferric chloride (Found: C, 65·8; H, 7·1. $C_{16}H_{20}O_5$ requires C, 65·9; H, 6·9%). Hydrolysis of the *ester* (3·5 g.) by heating it with 10% aqueous potassium hydroxide solution (40 ml.) yielded β-phenylacetylpropionic acid (2·2 g.), which crystallised from chloroform–light petroleum (b. p. 40—60°) in needles, m. p. 55° [Found: C, 68·6; H, 6·3%; *M* (by titration), 191·6. Calc. for $C_{11}H_{12}O_3$: C, 68·8; H, 6·3%; *M*, 192·1]. Its semicarbazone crystallised from dilute alcohol in needles, m. p. 183° (Found: C, 58·2; H, 6·1; N, 16·5. Calc. for $C_{12}H_{15}O_3N_3$: C, 57·8; H, 6·0; N, 16·85%).

Ethyl α-Phenylacetylglutarate (*Ethyl 4-Carbethoxy-5-keto-6-phenylhexanoate*).—Prepared by the action of ethyl β-iodopropionate (1 mol., 22·2 g.) on the sodio-derivative (1 mol.) of ethyl γ-phenylacetoacetate (20·6 g.) in absolute alcohol, this *ester*, when fractionated (22 g.), had b. p. 200—204°/6 mm., and gave a violet-red colour with ferric chloride (Found: C, 66·9; H, 7·0. $C_{17}H_{22}O_5$ requires C, 66·6; H, 7·2%).

γ-Phenylacetylbutyric Acid.—Hydrolysis (5 hours' heating) of the foregoing ester (3 g.) with 10% aqueous potassium hydroxide solution (30 ml.) and acidification precipitated the *acid* (2 g.), which crystallised from hot water in needles, m. p. 58° [Found: C, 70·1; H, 6·7%; *M* (by titration), 207·2. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%; *M*, 206·1]. Its *semicarbazone* crystallised from dilute alcohol in needles, m. p. 173° (Found: C, 59·5; H, 6·5; N, 15·5. $C_{13}H_{17}O_3N_3$ requires C, 59·3; H, 6·5; N, 15·6%).

Ethyl α-Diphenylmethyl-γ-phenylacetoacetate.—Diphenylmethyl bromide (1 mol., 12·4 g.) was heated with solid ethyl sodio-γ-phenylacetoacetate (1 mol., 11·5 g.) in benzene for 4 hours. The oily residue left after distillation of benzene solidified on cooling and yielded a crystalline solid (12 g.) on treatment with cold methanol. The solid gave a negative ferric chloride test, whereas the methanolic liquor gave a violet-red colour. The solid *ester* crystallised from alcohol in prisms, m. p. 112°, which dissolved readily in concentrated sulphuric acid, giving a red solution having a green fluorescence (Found: C, 80·6; H, 6·5; OEt, 11·8. $C_{25}H_{24}O_3$ requires C, 80·6; H, 6·5; OEt, 12·1%).

Benzyl 2 : 2-Diphenylethyl Ketone.—The foregoing ester (3 g.) was refluxed with 5% alcoholic potassium hydroxide solution (30 ml.) for 3 hours. The residue left after distillation of alcohol was mixed with water and extracted with ether. After distillation of ether, the oily residue solidified on cooling and the *ketone* crystallised from light petroleum (b. p. 40—60°) in fine needles, m. p. 72° (Found: C, 88·1; H, 6·8. $C_{22}H_{20}O$ requires C, 88·0; H, 6·7%). Its *oxime* crystallised from light petroleum in needles, m. p. 124° (Found: C, 83·9; H, 6·7; N, 4·3. $C_{22}H_{21}ON$ requires C, 83·8; H, 6·7; N, 4·4%). The alkaline solution left after extraction of the ketone was evaporated to dryness, and the residue digested with alcohol. The residue left after evaporation of the alcoholic extract yielded on acidification ββ-diphenylpropionic acid, which crystallised from dilute alcohol in needles, m. p. and mixed m.p. 154° (cf. Henderson, *loc. cit.*).

The γ-Lactone (IIa, or *b*).—Ice-cold concentrated sulphuric acid (40 ml.) was gradually added to ethyl phenylacetylsuccinate (15 g.), and the solution kept at 40° for 4 hours and at room temperature for 24 hours and then poured on ice. The brownish, sticky mass which separated was extracted with ether, and the ethereal solution dried. The viscous residue (8 g.) which was recovered from the ethereal solution was treated with benzene and thus separated into a pinkish crystalline solid (3 g.) and a brownish mother-liquor. The solid *lactone*, m. p. 165—170°, was freed from a water-soluble impurity by washing it with hot water. It crystallised from dilute methanol in plates, m. p. 218° (decomp.) (Found: C, 72·4; H, 4·2. $C_{12}H_8O_3$ requires C, 72·0; H, 4·0%), which gave a red colour with aqueous potassium hydroxide solution. Its *monoacetate* was prepared by heating the lactone (0·5 g.) with acetic anhydride (5 ml.) and fused sodium acetate (0·5 g.) for 2 hours on the steam-bath, and crystallised from methanol in needles, m. p. 155° (Found: C, 69·0; H, 4·0. $C_{14}H_{10}O_4$ requires C, 69·2; H, 4·1%).

Methanolysis. A solution of the lactone (0·5 g.) in 10 ml. of methanol was cooled in ice and then saturated with hydrogen chloride; after 3 hours at room temperature, the *methyl* ester (IVa or *b*) was precipitated by dilution with water. It crystallised from dilute methanol and recrystallised from light petroleum (b. p. 40—60°) in needles, m. p. 120° (Found: C, 68·4; H, 5·7; OMe, 23·8. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·8; 2OMe, 25·2%). Its *monoacetate* crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 83° (Found: C, 66·5; H, 5·6. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%).

3-*Hydroxy*-1 : 4-*naphthaquinone*-2-*acetic Acid.*—When a solution of the above-mentioned lactone (0·5 g.) in 5 ml. of alcohol was mixed with 15 ml. of 5% alcoholic potassium hydroxide solution, and the mixture exposed to air for 2 days, the red potassium salt separated; it was dissolved in water, and the solution acidified, and the resulting yellow quinone (0·5 g.) crystallised from water in golden-yellow plates, m. p. 208° (decomp.) (Found: C, 62·0; H, 3·5. Calc. for $C_{12}H_8O_5$: C, 62·0; H, 3·5%). Its methyl ester was prepared by the action of hydrogen chloride on a methanolic solution of the quinone, and crystallised from dilute methanol in lemon-yellow needles, m. p. 145° (Found: C, 63·0; H, 4·0; OMe, 11·8. Calc. for $C_{13}H_{10}O_5$: C, 63·3; H, 4·1; OMe, 12·6%). Decarboxylation of the acid with copper–barium chromite catalyst (Adkins, Connor, and Folkers, *J. Amer. Chem. Soc.*, 1932, **54**, 1138 in diphenyl ether yielded 3-hydroxy-2-methyl-1 : 4-naphthaquinone (Soliman and Latif, *loc. cit.*), m. p. and mixed m. p. 174°. More quinone was obtained by oxidation of the brownish residue recovered from the benzene mother-liquor left after isolation of the lactone. The crude quinone (1·8 g.), m. p.

170—180°, was digested with warm ether and the insoluble residue, m. p. 200°, was further purified by crystallisation from water.

δ-Lactone (V*a* or *b*).—Ethyl α-phenylacetylglutarate (12 g.) was dissolved in 35 ml. of ice-cold concentrated sulphuric acid, and the solution kept at 40° for 4 hours and at room temperature for 24 hours, then poured on ice; the brownish sticky product was extracted with ether and the residue (6·5 g.) recovered from the ethereal solution yielded a crystalline *lactone* (3·5 g.) on treatment with benzene. It crystallised from benzene in glistening plates, m. p. 175°, which lost their lustre on dehydration over phosphoric oxide (Found: C, 73·0; H, 4·7. $C_{12}H_{10}O_3$ requires C, 72·9; H, 4·7%). Its *monoacetate* crystallised from methanol in long needles, m. p. 147° (Found: C, 70·4; H, 4·8. $C_{14}H_{12}O_4$ requires C, 70·3; H, 4·7%).

Methanolysis. An ice-cold solution of the lactone (0·5 g.) in 10 ml. of methanol was saturated with hydrogen chloride, and after 3 hours at room temperature the *methyl methoxy*-ester was precipitated by dilution with water. It crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 103° (Found: C, 69·3; H, 6·1; OMe, 23·3. $C_{15}H_{16}O_4$ requires C, 69·2; H, 6·1; 2OMe, 23·8%).

2-*Hydroxy*-1 : 4-*naphthaquinone*-2-β-*propionic Acid.*—Prepared by oxidation of a solution of the δ-lactone (0·5 g.) in 5% alcoholic potassium hydroxide (15 ml.) by 2 days' exposure to air, the quinone crystallised from water in needles, m. p. 195° (Found: C, 63·6; H, 4·0. Calc. for $C_{13}H_{10}O_5$: C, 63·4; H, 4·1%). Its methyl ester, prepared by the action of hydrogen chloride and methanol, crystallised from alcohol in yellow needles, m. p. 138° (Found: C, 64·4; H, 4·7. Calc. for $C_{14}H_{12}O_5$: C, 64·4; H, 4·6%). More of the quinone was obtained as for the lower homologue. The crude quinone (1·7 g.) was digested with hot benzene, and the insoluble fraction was further purified by crystallisation.

2-*Carbethoxy*-3-*hydroxy*-1 : 4-*naphthaquinone.*—Oxidation of a solution of 2-carbethoxy-1 : 3-dihydroxynaphthalene (1 g.) in 20 ml. of 3% alcoholic potassium hydroxide by 2 days' exposure to air afforded an orange-yellow potassium salt; on acidification this gave the quinone (0·7 g.), which crystallised from ethyl acetate (slow evaporation) in prisms, and recrystallised from light petroleum (b. p. 40—60°) in orange plates, m. p. 110° (Found: C, 63·1; H, 4·2; OEt, 17·8. Calc. for $C_{13}H_{10}O_5$: C, 63·4; H, 4·1; OEt, 18·3%).

FAROUK I UNIVERSITY, MOHARRAM BEY, ALEXANDRIA. [*Received, September 12th,* 1950.]

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21. *Pteridines. Part I. An Unambiguous Synthesis of 7 : 8-Dihydro-6-hydroxypteridines.*

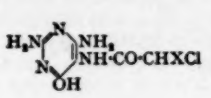
By W. R. BOON, W. G. M. JONES, and G. R. RAMAGE.

Condensation of 4-chloro-5-nitropyrimidines with an α-amino-acid ester readily yields 5-nitro-4-pyrimidylaminoacetic acid esters. Reduction of these compounds followed by loss of alcohol from the resultant 5-amino-compounds offers an unambiguous route to the synthesis of a large number of 7 : 8-dihydro-6-hydroxypteridines.

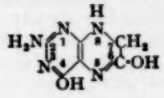
NEARLY all the methods available for the synthesis of pteridine derivatives involve the condensation of 4 : 5-diaminopyrimidines with α-diketones, α-keto-acids, α-ketols, or related substances. (For a review of the earlier literature see *Ann. Reports*, 1946, **43**, 250; 1948, **45**, 226.) Unless a symmetrical α-diketone is employed in such syntheses there is always an element of ambiguity about the structure of the resulting products. When 2 : 4 : 5-triamino-6-hydroxypyrimidine is used as the starting material it is frequently possible to check the constitution of the product by degradation to 2-amino-4-hydroxypteridine-6- or -7-carboxylic acid, both of which were prepared and characterised unambiguously by degradation during the determination of the structure of pteroylglutamic acid (Mowat *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 14). In other cases degradation to a pyrazine derivative has been employed (Weijlard, Tishler, and Erickson, *ibid.*, 1945, **67**, 802; Cain, Mallette, and Taylor, *ibid.*, 1948, **70**, 3026). Neither of these methods of orientation is readily extended to other classes of pteridine derivatives since, in many cases, it would prove difficult to obtain the necessary reference compounds by unambiguous synthesis.

There appear to be only two syntheses of pteridine derivatives by cyclisation of pyrimidine derivatives. Purrmann (*Annalen*, 1941, **546**, 98) condensed 2 : 4 : 5-triamino-6-hydroxypyrimidine with dichloroacetic acid and heated the silver salt of the resulting dichloroacetamide (I; X = Cl) with silver carbonate to obtain xanthopterin. In a similar manner Hitchings and Elion (*J. Amer. Chem. Soc.*, 1949, **71**, 467) treated the chloroacetamide (I; X = H) with sodium hydrogen carbonate and obtained a product to which they assign the structure (II) but which is different from the dihydroxanthopterin obtained by the reduction of xanthopterincarboxylic acid (Purrman, *Annalen*, 1941, **548**, 284), leucopterin (Totter, *J. Biol. Chem.*, 1944, **154**, 105), or xanthopterin (O'Dell, Vandenbelt, Bloom, and Pfiffner, *J. Amer. Chem. Soc.*, 1947, **69**, 250), and to which structure (II) has hitherto been assigned.

Timmis (*Nature*, 1949, **164**, 139) has described a method for the unambiguous synthesis of pteridine derivatives by condensation of 4-amino-5-nitrosopyrimidines with ketones, but only a few such pyrimidines can be prepared readily (Lythgoe, Todd, and Topham, *J.*, 1944, 315).



(I.)



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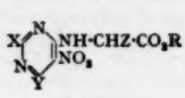


(III.)

This paper describes a method, first disclosed in B.P. 619,915, for the preparation of 7 : 8-dihydro-6-hydroxypteridines of unambiguous structure involving the reduction and subsequent cyclisation of α-(5-nitro-4-pyrimidylamino)-acid esters of type V. Waldmann (*J. pr. Chem.*, 1915, [ii], **91**, 193) has recorded a similar reaction in the preparation of 6-amino-1 : 2-dihydro-3-hydroxyquinoxaline by reduction of *N*-(2 : 4-dinitrophenyl)glycine or its ethyl ester. More recently Polonovski and Jérôme (*Compt. rend.*, 1950, **230**, 392), using essentially the procedure described in the above patent, prepared 2-amino-7 : 8-dihydro-6-hydroxy-4-methylpteridine from ethyl 2-amino-4-methyl-5-nitro-6-pyrimidylaminoacetate. The present paper describes a more extensive investigation of the scope of the method. Part II will record similar syntheses of other pteridine derivatives in which the first step is the condensation of an α-amino-ketone with a 4-chloro-5-nitropyrimidine (cf. B.P. 635,582; also Polonovski, Pesson, and Puister, *Compt. rend.*, 1950, **230**, 2205).

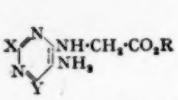
The initial experiments in this series employed as starting material 2 : 4-dichloro-6-methyl-5-nitropyrimidine readily available by the method of Baddiley and Topham (*J.*, 1944, 678). In later experiments 2 : 4-dichloro-5-nitro-, 4 : 6-dichloro-5-nitro-, and 4 : 6-dichloro-2-methyl-5-nitro-pyrimidine were also employed, these substances being obtained in a similar manner from the corresponding dihydroxy-compounds. Condensation of 2 : 4-dichloro-5-nitropyrimidine and the corresponding 4-methyl compound with glycine methyl or ethyl ester in cold methanol gave a mixture, readily separable by crystallisation, of the mono- (III; X = Cl, Y = H or Me, Z = H, R = Me or Et) and the di-esters (III; X = NH·CH_2·CO_2R, Y = H or Me, Z = H, R = Me or Et). If, however, an ethereal solution of the chloronitropyrimidine was shaken with an aqueous solution of glycine ester hydrochloride the monosubstituted product was obtained almost exclusively. With the 4 : 6-dichloropyrimidines even the latter method invariably gave a mixture. In a similar manner ethyl aminomalonate readily condensed with 2 : 4-dichloro-5-nitropyrimidine to give ethyl 2-chloro-5-nitro-4-pyrimidylaminomalonate (III; X = Cl, Y = H, Z = CO_2Et, R = Et).

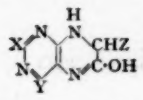
In all cases the second chlorine atom was readily replaced by an amino- or substituted amino-group, by reaction with ammonia or a primary or secondary amine. Its replacement by hydroxyl was best effected by a mild acid hydrolysis: for the 6-chloro-compounds a buffer of pH 5; for the 2-chloro-compounds *N*-acetic acid in presence of sodium acetate. More vigorous acid hydrolysis appeared to remove the amino-acid residue, and alkaline hydrolysis invariably gave highly coloured products.

2- or 4-Amino-5-nitropyrimidylaminoacetic esters have also been made by condensation of 2- or 4-amino-6-chloro-5-nitropyrimidines with glycine ester. 2-Amino-4-chloro-6-methyl-5-nitropyrimidine was readily obtained on heating 2-amino-4-hydroxy-6-methyl-5-nitropyrimidine with an excess of phosphorus oxychloride; the required 2-amino-5-nitro-6-methylpyrimidine was obtained by the nitration of 2-amino-4-hydroxy-6-methylpyrimidine, but not purified. 4-Amino-6-chloro-5-nitro- and 4-amino-6-chloro-2-methyl-5-nitro-pyrimidine were obtained by treating the appropriate dichloronitropyrimidine with cold aqueous ammonia. While 2-amino-4-chloro-6-methyl-5-nitropyrimidine condensed readily with glycine methyl ester, no reaction occurred between 2-amino-4-chloro-6-methylpyrimidine and glycine ethyl ester either in the cold, or in boiling ethanol; this is in line with Gabriel and Colman's observation (*Ber.*, 1899, **32**, 2923) that this substance was recovered unchanged after being heated under pressure with alcoholic ammonia; evidently the greater reactivity of the amino-acid ester is insufficient to overcome the lack of reactivity of the chlorine atom (which needs to be activated by a nitro-group).

Reduction of methyl 2-chloro-5-nitro-6-pyrimidylaminoacetate (III; X = Cl, Y = Z = H, R = Me) in methanolic solution by hydrogen in presence of Raney nickel gave methyl 5-amino-2-chloro-6-pyrimidylaminoacetate (IV; X = Cl, Y = H, R = Me), which, when boiled with water, preferably in an atmosphere of nitrogen, was converted into 2-chloro-7 : 8-dihydro-6-hydroxy-

pteridine (V; X = Cl, Y = Z = H). In the same manner ethyl 4-chloro-5-nitro-6-pyrimidylaminoacetate could also be reduced to the 5-aminopyrimidine which was subsequently cyclised to the corresponding pteridine.

(IV.) 

 (V.)

In all other cases in which X or Y was amino-, substituted amino-, or hydroxyl it was not possible readily to isolate the intermediate 5-aminopyrimidine compound on reduction. Frequently, however, in order to obtain good yields of the 6-hydroxypteridine it was necessary to heat the mixture under reflux in water.

Reduction and cyclisation of ethyl 2-hydroxy-4-methyl-5-nitro-6-pyrimidylaminoacetate gave 7 : 8-dihydro-2 : 6-dihydroxy-4-methylpteridine which however differed in both solubility and ultra-violet absorption from the substance obtained by Russell, Elion, and Hitchings (*J. Amer. Chem. Soc.*, **1949, 71**, 474).

Ultra-violet light absorption of 7 : 8-*dihydro*-6-*hydroxypteridines* (V).

Compound no.*	X.	Y.	0·1N-NaOH. $\lambda_{max.}$, mμ.	$\lambda_{min.}$, mμ.	ε.	0·1N-HCl. $\lambda_{max.}$, mμ.	$\lambda_{min.}$, mμ.	ε.
23	H	H	307	—	11,300	293	—	10,400
				253	1,700	—	245	1,100
24	Cl	H	310	—	12,000	295	—	10,600
				254	750	—	248	1,500
25	H	Cl	312	—	20,750	300	—	11,000
				260	2,700	—	247	1,250
27	Me	Cl	310	—	6,400	298	—	6,700
				257	375	—	248	700
28†	Cl	H	312	—	11,600	298	—	10,700
				260	1,100	—	252	1,000
29	NH_2	H	293	—	8,800	No maximum. End absorption (ε 13,500) at 230 mμ. Infln. at 265, 295 mμ.; ε 6,800, 4,900		
				253	1,300			
30	H	NH_2	295	—	10,200	287	—	11,700
				257	3,250	—	252	1,350
32	H	NEt_2	310	—	14,750	315	—	15,000
				280	4,200	—	275	3,100
33	Me	NEt_2	310	—	6,900	315	—	8,400
				275	2,700	—	272	2,000
34	NEt_2	Me	298	—	14,800	248	—	30,700
				263	4,900	Infl. 292	—	6,700
38	$Et_2N{\cdot}[CH_2]_2{\cdot}NH$	Me	298	—	13,700	232	—	21,700
				257	1,900	Infl. 285	—	1,900
39	OH	H	277	—	10,000	260	—	10,000
				258	4,200	—	285	3,300
						317	—	6,800
40	OH	Me	280	—	9,200	—	243	6,600
				257	4,900	265	—	9,200
			Infl. 310	—	5,700	—	288	3,100
						313	—	8,300
41	H	OH	275	—	6,300	—	245	2,100
				253	100	272	—	3,800
							295	2,000
						315	—	2,100
42	Me	OH	275	—	7,500	272	—	2,900
				250	1,900	—	—	—

* Cf. Tables I and II. † CO_2Et at position 7.

The influence of the nature of the substituents on the physical properties of the resulting pteridines is of particular interest. Compounds having a hydroxy- or an amino- or no substituent in the pyrimidine ring were, without exception, of very high melting point, insoluble in the usual organic solvents, but soluble to some extent in such high-boiling polar solvents as dimethylformamide and 2-ethoxyethanol. In a few cases the limited solubility in water per-

mitted recrystallisation for analyses but in others reprecipitation, usually by the addition of sodium acetate to a solution in dilute hydrochloric acid, was the only practicable method. In all cases drying at 120—150° over phosphoric oxide *in vacuo* was necessary if reliable analytical results were to be obtained. If the substituent in the pyrimidine portion of the molecule was 2'-diethylaminoethylamino-, the products were still fairly high melting but could be crystallised from polar solvents such as methanol and ethanol. A similar, though rather less marked, effect was brought about by the introduction of a carbethoxy-group in position 7. The presence of a diethylamino-group in the 2- and more particularly in the 4-position markedly lowered the melting point and rendered possible crystallisation from such non-polar solvents as benzene. This, no doubt, is a consequence of the greatly reduced possibilities for intermolecular hydrogen bonding.

Chlorine in the 2- or the 4-position of 7 : 8-dihydro-6-hydroxypteridines is practically inert and the compounds are similar to the unsubstituted compound; the only method so far found for the conversion of 2-chloro-7 : 8-dihydro-6-hydroxypteridine into the parent compound was reduction with hydriodic acid in presence of red phosphorus. The same product, giving an identical *X*-ray powder photograph, was obtained by a similar reduction of 4-chloro-7 : 8-dihydro-6-hydroxypteridine.

The ultra-violet light absorptions of most of the 7 : 8-dihydro-6-hydroxypteridines have been measured in solution in 0·1N-hydrochloric acid and in 0·1N-sodium hydroxide, using a Unicam photoelectric spectrophotometer (see Table).

Experimental.

4 : 6-*Dihydroxy-5-nitropyrimidine.*—Nitration of 4 : 6-dihydroxypyrimidine (Kenner, Lythgoe, Todd, and Topham, *J.*, 1943, 389) in concentrated sulphuric acid generally gave low and variable yields. The following procedure was readily reproducible on any scale: 4 : 6-Dihydroxypyrimidine (1 mol.) was added, with stirring, at 15—20° to a mixture of 93% nitric acid (3 mols.) and glacial acetic acid (6 mols.). Stirring was continued for a further half hour and the mixture then poured on ice. After filtration, washing with water, and drying, the product (90% yield) was pure enough for further use. The *nitro*-compound crystallised from water in colourless leaflets, m. p. >300° (Found: C, 30·8; H, 2·0; N, 26·3 $C_4H_3O_4N_3$ requires C, 30·6; H, 1·9; N, 26·8%).

4 : 6-*Dichloro-5-nitropyrimidine.*—Dimethylaniline (93 g., 0·77 mol.) was added to a suspension of 4 : 6-dihydroxy-5-nitropyrimidine (78·5 g., 0·5 mol.) in phosphorus oxychloride (505 g., 3·3 mols.) and heated in an oil-bath at 125—130° for 1 hour. After removal of the excess of phosphorus oxychloride under reduced pressure, the reaction mixture was poured on ice (800 g.) and filtered. The filtrate was extracted with ether (3 × 350 c.c.), each extract being also used to extract the filter cake. The combined extracts were washed with water (500 c.c.) and dried (Na_2SO_4) and the ether was removed. The residual *dichloro*-compound crystallised from light petroleum (b. p. 80—100°) (yield 82·5 g., 85%) (Found: C, 24·9; H, 0·6; N, 21·8; Cl, 36·4. $C_4HO_2N_3Cl_2$ requires C, 24·7; H, 0·5; N, 21·7; Cl, 36·6%).

2-*Amino-4-chloro-6-methyl-5-nitropyrimidine.*—2-Amino-4-hydroxy-6-methylpyrimidine (30 g.) was added in small portions during 45 minutes and below 10° to 100 c.c. of a mixture of equal volumes of fuming nitric acid and concentrated sulphuric acid. After 15 minutes at room temperature the mixture was poured on ice, and excess of aqueous ammonia added, followed by acetic acid until the whole was acid to litmus. The product (21 g.), filtered off and crystallised from a large volume of water, had m. p. 325—327° (decomp.). Satisfactory analytical results could not be obtained with this substance. When heated under reflux with excess of phosphorus oxychloride and then freed from the excess by distillation and basification with sodium carbonate, it was converted into 2-*amino-4-chloro-6-methyl-5-nitropyrimidine*, which had m. p. 225° after crystallisation from ethanol or, better, sublimation (Found: C, 32·1; H, 3·2; Cl, 19·1. $C_5H_5O_2N_4Cl$ requires C, 31·8; H, 2·7; Cl, 18·8%).

4-*Amino-6-chloro-5-nitropyrimidine.*—To 4 : 6-dichloro-5-nitropyrimidine (38·8 g., 0·2 mol.) dissolved in ether (300 c.c.) a solution of ammonia (6·9 g., 0·4 mol.) in methanol (30 c.c.) was added, with stirring, during 1 hour. After further hour's stirring the solid was filtered off, washed with ether, and extracted with hot ethyl acetate (2 × 100 c.c.). The solid, 4 : 6-*diamino-5-nitropyrimidine*, crystallised from acetic acid, had m. p. >250° (Found: C, 31·1; H, 2·9. $C_4H_5O_2N_5$ requires C, 30·9; H, 3·2%). The united residues obtained by concentration of the ether–methanol filtrate and the ethyl acetate extract were extracted with hot light petroleum (b. p. 60—80°; 2 × 50 c.c.) to remove unchanged 4 : 6-dichloro-5-nitropyrimidine (4·3 g.). The residue, on crystallisation from benzene, gave 4-*amino-6-chloro-5-nitropyrimidine* (17·3 g., 54%), m. p. 155—156° (Found: C, 27·7; H, 1·5; N, 32·1; Cl, 20·0. $C_4H_3O_2N_4Cl$ requires C, 27·5; H, 1·7; N, 32·1; Cl, 20·3%).

4-*Amino-6-chloro-2-methyl-5-nitropyrimidine*, m. p. 183° (from xylene) (Found: C, 31·8; H, 2·65; N, 29·8; Cl, 18·8. $C_5H_5O_2N_4Cl$ requires C, 31·8; H, 2·7; N, 29·8; Cl, 18·8%), was obtained similarly from 4 : 6-dichloro-2-methyl-5-nitropyrimidine.

2- *and* 4-*Chloro-5-nitro-6-pyrimidylaminoacetic Esters* (*Method* I).—The two methods which have been used for the preparation of these substances are exemplified by the following details for the preparation of *methyl* 2-*chloro-5-nitro-6-pyrimidylaminoacetate*.

(*a*) A solution of sodium methoxide [from 4·6 g. (0·2 mol.) of sodium in 120 c.c. of methanol] was added to glycine ester hydrochloride (25·1 g., 0·2 mol.) in methanol (75 c.c.). After removal of the sodium chloride by filtration the solution was added below 0°, with stirring, to 2 : 6-dichloro-5-nitropyrimidine

(19·4 g., 0·1 mol.) in methanol (50 c.c.). 15 Minutes after the addition was complete the product was filtered off; it crystallised from methanol in needles, m. p. 108° (14 g., 56·8%) (Found: C, 34·0; H, 3·0; N, 22·5. $C_7H_7O_4N_4Cl$ requires C, 34·1; H, 2·8; N, 22·7%). Some 2 : 6-*biscarbomethoxymethylamino-5-nitropyrimidine*, m. p. 153° (from 2-ethoxyethanol) (Found: C, 40·1; H, 4·4. $C_{10}H_{13}O_8N_5$ requires C, 40·1; H, 4·3%), was also obtained.

(*b*) To an ice-cold solution of 2 : 6-dichloro-5-nitropyrimidine (10 g., 0·05 mol.) in ether (50 c.c.) and a suspension of sodium hydrogen carbonate (16 g.) in water (50 c.c.) finely powdered glycine methyl ester hydrochloride (10 g., 0·08 mol.) was added slowly with constant shaking. The crystalline product (9 g., 73%) which separated was dried and crystallised from light petroleum (b. p. 100—120°).

In general, method (*b*) is preferred as it reduces very considerably the tendency to disubstitution; even so, the isolation of monosubstitution products from the 4 : 6-dichloro-5-nitropyrimidines is difficult. Details of the preparations are given in Table I (compounds 1—7).

2- *and* 4-*Amino-* (*and Substituted-Amino-*)5-*nitro*-6-*pyrimidylaminoacetic Esters* (*Method II*).—These were made either (*a*) by treating the appropriate chloro-5-nitro-6-pyrimidylaminoacetic ester with excess (<2 mols.) of ammonia or a base or (*b*), for the amino-compounds only, by treating a 2-amino-4-chloro-5-nitro- or 4-amino-2-chloro-5-nitro-pyrimidine with a glycine ester. In the case (*c*) where the substituted amino-group is a second aminoacetic ester residue the compounds have also been made by treating the 2 : 4- or 4 : 6-dichloro-5-nitropyrimidine with an excess of glycine ester.

Ethyl 2-*amino*-4-*methyl*-5-*nitro*-6-*pyrimidylaminoacetate*.—(*a*) *From ethyl* 2-*chloro*-4-*methyl*-5-*nitro*-6-*pyrimidylaminoacetate*. The chloro-ester (5·5 g., 0·02 mol.) in ethanol (30 c.c.) was cooled in ice and 6N-ethanolic ammonia (20 c.c.) added. After 1 hour the solid *pyrimidylaminoacetate* which separated was filtered off, washed with water, and crystallised from ethanol. It (4·6 g., 90%) had m. p. 187° (Found: C, 42·6; H, 5·1; N, 27·6. $C_8H_{13}O_4N_5$ requires C, 42·4; H, 5·1; N, 27·4%).

(*b*) To 2-amino-4-chloro-6-methyl-5-nitropyrimidine (3·8 g., 0·02 mol.) in ether (50 c.c.), glycine ester (2·5 g., 1·025 mol.) was added. After 1 hour the solid was collected, washed with water, and crystallised from ethanol to give the foregoing product (m. p. and mixed m. p.).

(*c*) 2 : 6-*Biscarbomethoxymethylamino*-5-*nitropyrimidine*. To 2 : 6-dichloro-5-nitropyrimidine (1·97 g., 0·01 mol.) in methanol (5 c.c.) a methanol solution of glycine methyl ester (3·5 g., 0·04 mol.) was added. The crystalline *product* which slowly separated was filtered off, washed with water, and crystallised from methanol. It (1·6 g., 55%) had m. p. 153° (Found: C, 40·1; H, 4·4. $C_{10}H_{13}O_8N_5$ requires C, 40·5; H, 4·3%). The same product was obtained from methyl 2-chloro-5-nitro-6-pyrimidylaminoacetate and glycine methyl ester in methanol.

Details of products of this type are given in Table I (compounds 8—22).

2- *and* 4-*Hydroxy*-5-*nitro*-6-*pyrimidylaminoacetic Esters* (*Method III*).—*Ethyl* 2-*hydroxy*-5-*nitro*-6-*pyrimidylaminoacetate*. Ethyl 2-chloro-5-nitro-6-pyrimidylaminoacetate (28 g., 0·1 mol.), N-acetic acid (400 c.c.), and fused sodium acetate (8·5 g.) were heated under reflux for 1 hour in a stream of nitrogen. Charcoal was then added and the whole filtered. On cooling, 7·7 g. of *hydroxy*-compound separated; a further 4·9 g. separated on concentration. Crystallised from water, it had m. p. 230—232° (decomp.) after sintering at 225° (Found: C, 40·0; H, 4·2; N, 23·3. $C_8H_{10}O_5N_4$ requires C, 39·6; H, 4·1; N, 23·2%).

Methyl 2-*hydroxy*-4-*methyl*-5-*nitro*-6-*pyrimidylaminoacetate*, m. p. >240° (Found: C, 39·9; H, 4·4; N, 23·0. $C_8H_{10}O_5N_4$ requires C, 39·6; H, 4·1; N, 23·2%), was obtained similarly from methyl 2-chloro-5-nitro-4-methyl-6-pyrimidylaminoacetate.

Ethyl 4-*hydroxy*-5-*nitro*-6-*pyrimidylaminoacetate*, obtained in 45% yield by heating the chloro-compound with 0·2M-acetate buffer (pH 5) for 3 hours on the steam-bath, had m. p. 214° (decomp.) (Found: C, 39·7; H, 3·8; N, 23·3%). Methyl 2-chloro-5-nitro-6-pyrimidylaminoacetate was hydrolysed by moist air to *methyl* 4-*hydroxy*-2-*methyl*-5-*nitro*-6-*pyrimidylaminoacetate*, m. p. 230° (decomp.) (Found: C, 40·2; H, 4·1; N, 23·1%).

Methyl 5-*Amino*-2-*chloro*-6-*pyrimidylaminoacetate*.—Methyl 2-chloro-5-nitro-6-pyrimidylaminoacetate (6 g.) in methanol (400 c.c.) was reduced with hydrogen at room temperature and a pressure of 60 lb./sq.in. in presence of Raney nickel and calcium carbonate. After filtration, dilution with water (200 c.c.) and long storage the 5-*amino*-ester separated in fine yellow needles. Crystallised from xylene, it was obtained colourless and having m. p. 142° (Found: C, 39·3; H, 4·3; N, 25·4. $C_7H_9O_2N_4Cl$ requires C, 38·8; H, 4·2; N, 25·8%).

Ethyl 5-*Amino*-4-*chloro*-6-*pyrimidylaminoacetate*.—After reduction and filtration as above, the methanol was removed under reduced pressure and the residue extracted with ethyl acetate. Removal of the ethyl acetate and crystallisation of the residue first from benzene and then from hexane gave the *amino*-compound, m. p. 133° (Found: C, 41·9; H, 4·8; N, 24·0; Cl, 15·2. $C_8H_{11}O_2N_4Cl$ requires C, 42·1; H, 4·8; N, 24·3; Cl, 15·4%).

7 : 8-*Dihydro*-6-*hydroxypteridines*.—In general these substances were prepared by hydrogenation in presence of Raney nickel of the appropriate 5-nitro-6-pyrimidylaminoacetic esters in methanol. After removal of the catalyst by filtration or flotation it was sometimes necessary, particularly with the chloro-compounds, to complete the ring closure by heating the product under reflux in presence of water and in an atmosphere of nitrogen. Substances with suitable substituents, *e.g.*, diethylamino-, were reasonably soluble in organic solvents and could be purified by crystallisation. In other cases purification was effected by dissolution in dilute hydrochloric acid, treatment with charcoal, and precipitation by sodium acetate. Details and analyses are given in Table II.

7 : 8-*Dihydro*-6-*hydroxypteridine*.—2-Chloro-6-hydroxy-7 : 8-dihydropteridine (1 g.), hydriodic acid (*d* 1·7; 6 c.c.), and red phosphorus (1 g.) were heated at 160° for 1 hour. After cooling and filtration, the

TABLE I.

5-Nitro-6-pyrimidylaminoacetic esters (IV).

Compound no.	X.	Y.	R.	Method of prepn.	Yield, %.	Solvent.†	M. p.	Formula.	Found, %. C.	H.	N.	Required, %. C.	H.	N.
1	Cl	H	Me	Ia (Ib)	56·8 (73)	Petrol (100—120°)	108°	$C_7H_7O_4N_4Cl$	34·0	3·0	22·5	34·1	2·8	22·7
2	Cl	H	Et	Ib	71	C_6H_6	101—102	$C_8H_9O_4N_4Cl$ ‡	37·2	3·2	21·3	36·9	3·5	21·5
3	H	Cl	Et	Ib	31	Petrol (60—80°)	93—94	$C_8H_9O_4N_4Cl$ ‡	37·1	3·3	21·4	36·9	3·5	21·5
4 •	Cl	H	Et	Ib	52·5	EtOH	86	$C_{11}H_{15}O_8N_4Cl$	40·0	3·9	16·7	39·7	3·9	16·8
5	Cl	Me	Me	Ia (Ib)	53 (75)	EtAc	(102)	$C_8H_9O_4N_4Cl$	37·0	3·6	21·5	36·9	3·5	21·5
6	Cl	Me	Et	Ia	69	EtOH	79	$C_9H_{11}O_4N_4Cl$	39·2	4·1	20·2	39·3	4·0	20·4
7	Me	Cl	Me	Ib	43	Petrol (60—80°)	104	$C_8H_9O_4N_4Cl$ ‡	36·7	3·2	21·8	36·9	3·5	21·5
8	NH·CH_2·CO_2Me	H	Me	Ia (IIc)	(55)	MeOH	153	$C_{10}H_{13}O_6N_5$	40·1	4·4	—	40·1	4·3	—
9	H	NH·CH_2·CO_2Et	Et	Ib	—	EtOH	143	$C_{12}H_{17}O_6N_5$	43·6	5·0	20·9	44·0	5·2	21·4
10	NH·CH_2·CO_2Me	Me	Me	IIc	55	MeOH	152	$C_{11}H_{15}O_6N_5$	42·1	4·9	23·0	42·2	4·8	22·4
11	Me	NH·CH_2·CO_2Me	Me	Ib	—	EtAc	165	$C_{11}H_{15}O_6N_5$	42·2	4·9	22·0	42·2	4·8	22·4
12	NH_2	H	Me	IIa	50	EtO·$[CH_2]_2$·OH	210	$C_7H_9O_4N_5$	37·0	4·1	30·5	37·0	4·0	30·8
13	NH·$[CH_2]_2$·NEt_2	H	Me	IIa	68	MeOH–H_2O	108	$C_{12}H_{22}O_4N_6$	47·5	6·5	25·4	47·8	6·7	25·8
14	H	NH_2	Et	IIa (IIb)	83	EtOH	166	$C_8H_{11}O_4N_5$	40·0	4·6	28·6	39·8	4·6	29·0
15	H	NEt_2	Et	IIa	80	Petrol (80—100°)	78·5	$C_{12}H_{19}O_4N_5$	48·8	6·5	23·6	48·5	6·4	23·6
16 •	NEt_2	H	Et	IIa	90	EtOH	98	$C_{12}H_{23}O_4N_5$	48·8	6·4	19·2	48·8	6·2	19·0
17	NH_2	Me	Me	IIa (IIb)	90	MeOH	187	$C_9H_{13}O_4N_5$	42·6	5·1	27·6	42·4	5·1	27·5
18	NEt_2	Me	Me	IIa	84	MeOH	100·5	$C_{12}H_{19}O_4N_5$	48·5	6·3	23·7	48·5	6·4	23·6
19	NH·$[CH_2]_2$·NEt_2	Me	Me	IIa	51	Petrol (60—80°)	83	$C_{14}H_{24}O_4N_6$	49·2	6·7	24·8	49·4	7·1	24·7
20	Me	NH_2	Me	IIb	65	Dioxan	239	$C_8H_{11}O_4N_5$	40·0	5·0	29·3	39·8	4·6	29·0
21	Me	NEt_2	Me	IIa	58	Petrol (60—80°)	77	$C_{12}H_{19}O_4N_5$	48·6	6·3	23·8	38·5	6·4	23·6
22	Me	NH·$[CH_2]_2$·NEt_2	Me	IIa	—	Petrol (60—80°)	82	$C_{14}H_{24}O_4N_6$	49·4	6·8	24·3	49·4	7·1	24·7

• Side-chain NH·CH(CO_2Et)$_2$ in place of NH·CH_2·CO_2R.

† Petrol = light petroleum of the b. p. stated in parentheses.

‡ Found : Cl (No. 2) 13·7, (No. 3) 13·5, (No. 7) 13·3. Required : Cl, 13·6%.

TABLE II.

6-Hydroxy-7 : 8-dihydropteridines (V).

Compound no.	X.	Y.	Purification.	M. p.†	Formula.	Found, %. C.	H.	N.	Required, %. C.	H.	N.
23	H	H	H_2O	>400°	$C_6H_4ON_4$	47·9	4·2	37·3	48·0	4·0	37·3
24	Cl	H	Pptn.	>400	$C_6H_3ON_4Cl$	39·3	3·1	30·4	39·0	2·7	30·4
25	H	Cl	H_2O	>400	$C_6H_3ON_4Cl$ ‡	39·4	2·9	30·6	39·0	2·7	30·4
26	Cl	Me	EtO·$[CH_2]_2$·OH	>400	$C_7H_7ON_4Cl$ §	42·5	3·7	28·8	42·3	3·5	28·2
27	Me	Cl	H_2O	>400	$C_7H_7ON_4Cl$ §	41·5	3·9	27·6	42·3	3·5	28·2
28 •	Cl	H	Aq. NH_3	239	$C_9H_9O_5N_4Cl$	42·2	3·9	21·8	42·1	3·5	21·8
29	NH_2	H	80% HCO_2H	>250	$C_6H_7ON_5$,$2H_2O$	35·7	5·6	34·8	35·8	5·5	34·8
30	H	NH_2	H_2O	>250	$C_6H_7ON_5$	43·7	3·9	41·9	43·6	4·2	42·4
31	Me	NH_2	Pptn.	>400	$C_7H_9ON_5$	46·5	5·2	39·2	46·9	5·0	39·1
32	H	NEt_2	C_6H_6	197—199	$C_{10}H_{15}ON_5$	54·2	6·6	31·2	54·3	6·8	31·6
33	Me	NEt_2	C_6H_6	208	$C_{11}H_{17}ON_5$	56·0	7·2	30·3	56·2	7·2	29·8
34	NEt_2	Me	MeOH	284	$C_{11}H_{17}ON_5$	56·2	7·1	29·6	56·2	7·2	29·8
35 •	NEt_2	H	EtO·$[CH_2]_2$·OH	212 (d)	$C_{12}H_{19}O_3N_5$	52·9	6·4	—	53·2	6·5	23·9
36	MeO_2C·CH_2·NH	H	EtO·$[CH_2]_2$·OH	290 (d)	$C_9H_{11}O_3N_5$	45·4	4·9	29·6	45·6	4·6	29·5
37	Et_2N·$[CH_2]_2$·NH	H	EtOH	204	$C_{12}H_{20}ON_6$	54·1	7·5	31·9	54·5	7·6	31·8
38	Et_2N·$[CH_2]_2$·NH	Me	MeOH	243	$C_{13}H_{22}ON_6$	56·4	7·8	30·5	56·1	7·9	30·2
39	OH	H	Pptn.	>300	$C_6H_4O_2N_4$	43·6	3·6	33·8	43·4	3·6	33·7
40	OH	Me	Pptn.	>300	$C_7H_6O_2N_4$	46·0	4·6	30·4	46·6	4·4	31·1
41	H	OH	Pptn.	>300	$C_6H_4O_2N_4$	43·6	3·8	33·8	43·4	3·6	33·7
42	Me	OH	H_2O	>300	$C_7H_6O_2N_4$	46·9	4·6	30·9	46·6	4·4	31·1

• 7-Carbethoxy-derivative.

† (d) = with decomposition.

‡ Found : Cl, 18·5. Required : Cl, 19·3%.

§ Found : Cl (No. 26), 18·5, (No. 27) 17·4. Required : Cl, 17·9%.

filtrate was made strongly alkaline by 20% sodium hydroxide solution. The crystalline sodium salt which separated on cooling was dissolved in water, and acidified to Congo-red with hydrochloric acid. The whole was heated with charcoal, filtered, and reprecipitated by the addition of sodium acetate. 7 : 8-*Dihydro-6-hydroxypteridine* (0·7 g.) was filtered off, washed, and dried at 120° *in vacuo*; it did not melt below 300° (Found : C, 48·2; H, 3·9; N, 37·4. $C_6H_5ON_4$ requires C, 48·0; H, 4·0; N, 37·3%). The same substance was prepared similarly from 4-chloro-6-hydroxy-7 : 8-dihydropteridine (Found : C, 47·9; H, 4·2; N, 37·3%).

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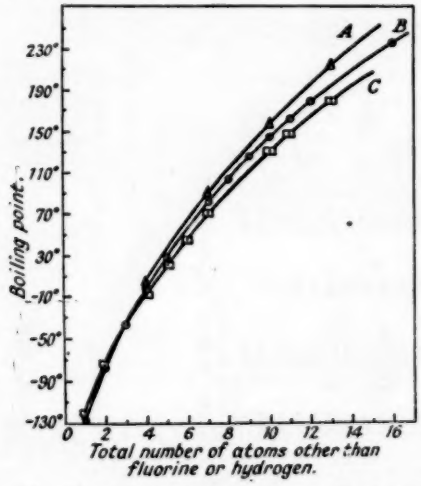
22. *Perfluoro*-tert.-*amines.*

By R. N. HASZELDINE.

The passage of tertiary amines over cobalt trifluoride gives the corresponding perfluoro-*tert.*-amines in small yield. The physical properties of these compounds are compared with those of fluorocarbons of similar volatility.

THE interaction of nitrogen-containing organic compounds and fluorine on the surface of gold-plated copper turnings, or the passage of such compounds over heated cobalt trifluoride has been shown to yield the corresponding perfluoro-compounds (Haszeldine, *J.*, 1950, 1966). A series of perfluoro-*tert.*-amines whose properties are very similar to fluorocarbons of comparable boiling point has now been prepared.



A : Tertiary amines, $C_nH_{2n+3}N$. *B : Fluorocarbons*,* $C_{n+1}F_{2n+4}$. *C : Perfluoro*-tert.-*amines*, $C_nF_{2n+3}N$.

* The boiling-point data for the fluorocarbons are from Haszeldine and Smith (*J.*, in the press).

The fluorination of the tertiary amines was accompanied by extensive decomposition and possibly by rearrangement, and the low yields of the perfluoro-*tert.*-amines are attributed in part to non-volatile hydrofluoride formation. The product from trimethylamine contained only small amounts of perfluorotrimethylamine and somewhat larger amounts of perfluorodimethylamine, perfluoromethylamine, and higher-boiling, completely fluorinated compounds, some of which may be cyclic. The products from the higher tertiary amines were complex, and only the material corresponding to the perfluoro-*tert.*-amine was therefore isolated.

The seven perfluoro-compounds prepared were : $N(CF_3)_3$, $N(CF_3)_2(C_2F_5)$, $N(CF_3)(C_2F_5)_2$, $N(C_3F_7)_3$, $N(C_3F_7)_2(is)$-C_4F_9), and $N(C_4F_9)_3$. The boiling points of these compounds lie on a smooth curve, and NF_3, b. p. −120°, $NF(CF_3)_2$, b. p. −37° (Haszeldine, *loc. cit.*; Emeléus and Thompson, *J.*, 1949, 3080), and $NF_2{\cdot}CF_3$, b. p. −75° (Haszeldine, *loc. cit.*), lie on a con-

tinuation of this curve as shown in the diagram. The boiling points of the parent tertiary amines are also recorded and are seen to lie substantially above those of the fluorinated compounds. A comparison of the boiling points of the fluorocarbons and the perfluoro-*tert.*-amines reveals that the latter, $C_nF_{2n+3}N$, have a volatility similar to the fluorocarbons, $C_{n+1}F_{2n+4}$, derived from the *n*-paraffins. Hence, replacement of a carbon atom in a fluorocarbon by nitrogen, although it gives a compound containing one less fluorine atom, has little effect on the boiling point. This effect was noted earlier (Haszeldine, *loc. cit.*) with perfluoropiperidine and perfluoro*cyclo*hexylamine, and would indicate that the compound, m. p. 94—95°, originally believed to be perfluorodimethylpiperidine (Haszeldine, *J.*, 1950, 1638), was incompletely fluorinated and contained one hydrogen atom, since the perfluoro-compound would be expected to boil in the region 90—100°.

Carbon tetrafluoride and hexafluoroethane have boiling points slightly below nitrogen trifluoride and perfluoromethylamine; the boiling points of octafluoropropane and perfluorodimethylamine are almost identical, and above this point the two curves gradually diverge with increase in molecular weight, but even when $n = 9$ (perfluorodecane) the difference in boiling point in the two series is only 15°. The boiling points of perfluoropiperidine and perfluoro*cyclo*hexylamine lie between the two curves.

The refractive indices (n_D) and densities (g./c.c.), both at 25°, of the perfluoro-*tert.*-amines are also similar to those of the fluorocarbons; *e.g.*, C_7F_{16}, n 1·267, d 1·741, and $N(C_3F_8)_3$, n 1·262, d 1·736; $C_{10}F_{22}$, n 1·279, d 1·816, and $N(C_3F_7)_3$, n 1·279, d 1·822; $C_{11}F_{24}$, n 1·286, d 1·857, and $N(C_3F_7)_2(iso\text{-}C_4F_9)$, n 1·283(5), d 1·84(1). The values of n_D^{25} and d_4^{25} for $C_{10}F_{22}$ and $C_{11}F_{24}$ are extrapolated from the data of Haszeldine and Smith (*J.*, in the press), since these fluorocarbons, unlike the nitrogen-containing compounds, are solids. The atomic refraction of fluorine, derived on the assumption that the atomic refraction of nitrogen is the same as in tertiary amines, is 1·21 (see table), a value similar to that derived from the fluorocarbons (Haszeldine and Smith, *loc. cit.*).

Chemically, the perfluoro-*tert.*-amines are inert like the fluorocarbons and show no basic character; like perfluoro*cyclo*hexylamine and perfluoropiperidine, they resemble nitrogen trifluoride.

Experimental.

Apparatus.—The cobalt fluoride apparatus and the technique employed were as described by Haszeldine (*loc. cit.*). A nitrogen stream of 10 l./hr. and a reaction temperature (not necessarily the best) of 250—350° were used, depending upon the b. p. of the compound under examination. Trimethyl-, triethyl-, tripropyl-, and tributyl-amine were studied in most detail, only small quantities of the other *tert.*-amines being available.

Fluorination of Trimethylamine.—Trimethylamine (5 ml./hr.) was passed over cobalt trifluoride kept at 250°. From a total of 100 g. of tertiary amine there were isolated : (*a*) perfluoromethylamine (1·6 g.) (Found : *M*, 119. Calc. for CNF_3 : *M*, 121), b. p. *ca.* −75° (Haszeldine, *loc. cit.*, reports b. p. −75°); (*b*) perfluorodimethylamine (4·1 g.) (Found : *M*, 170. Calc. for C_2NF_7 : *M*, 171), b. p. −38° to −35° (Emeléus and Thompson, *loc. cit.*, report b. p. −37·0°); (*c*) *perfluorotrimethylamine* (2·2 g.; 6%) (Found : C, 16·3; N, 5·9; F, 76·8%; *M*, 220. C_3NF_9 requires C, 16·3; N, 6·3; F, 77·4%; *M*, 221), b. p. −6° to −7°; (*d*) unidentified and possibly cyclic compounds with b. p.'s between 0° and 70°, one of which, b. p. 54—56° (cf. C_6F_{14}, b. p. 58°) may be *perfluorotetramethylhydrazine*, $(CF_3)_2N{\cdot}N(CF_3)_2$ (Found : N, 9·0%; *M*, 298. $C_4N_2F_{12}$ requires N, 9·2%; *M*, 304). The yields of the compounds given here are lower than the true yields because of the exhaustive fractionation required to separate them from partly fluorinated and degradation products.

Fluorination of Ethyldimethylamine.—A total of 52 g. of this amine, added at 4 ml./hr., was fluorinated at a temperature of 250°. *Perfluoroethyldimethylamine* (1·3 g.) (Found : C, 17·7; N, 5·5; F, 76·7%; *M*, 268. C_4NF_{11} requires C, 17·7; N, 5·2; F, 77·1%; *M*, 271), b. p. 20—22°, was isolated by fractionation of the product with b. p. >0°. In this and subsequent experiments, no attempt was made to separate the other, complex, reaction products.

Fluorination of Diethylmethylamine.—The amine (37 g.), passed over cobalt trifluoride at 3·5 ml./hr. at 260°, gave *perfluorodiethylmethylamine* (1·1 g.) (Found : C, 18·5; N, 4·3; F, 76·4%; *M*, 322. C_5NF_{13} requires C, 18·7; N, 4·35; F, 76·95%; *M*, 321), b. p. 45·5—46·5°.

Fluorination of Triethylamine.—Triethylamine (210 g.) was added at 5 ml./hr. to the reaction vessel heated initially to 270° and kept at this temperature throughout the reaction. *Perfluorotriethylamine* (6·3 g.), b. p. 69·8—71·0°, was isolated by fractional distillation (Found : C, 19·2; N, 3·5; F, 76·3%; *M*, 368. C_6NF_{15} requires C, 19·4; N, 3·8; F, 76·8%; *M*, 371). The vapour pressure, determined over the range 12—70°, is given by the equation $\log_{10} p = 7{\cdot}936 - 1736{\cdot}0/T$, whence the b. p. is calculated as 70·3°, the latent heat of vaporisation as 7940 cals./mole, and Trouton's constant as 23·1. Also determined were n_D^{18} 1·270, n_D^{25} 1·262, and d_4^{25} 1·736.

Fluorination of Tripropylamine.—Tripropylamine (196 g. at 5 ml./hr.) was passed over cobalt trifluoride at 300°, and yielded *perfluorotripropylamine* (7·1 g.) (Found : C, 20·6; N, 2·95; F, 76·1%; *M*, 515, 519. C_9NF_{21} requires C, 20·7; N, 2·8; F, 76·6%; *M*, 521), b.p. 129·5—130·5°, $n_D^{14.5}$ 1·284, n_D^{25} 1·279, d_4^{25} 1·822. The vapour-pressure equation, calculated from only six points measured in the

range 60—130°, is given by $\log_{10} p = 8{\cdot}143 - 2121{\cdot}0/T$, whence the calculated b. p. is 129·9° ±0·15°, the latent heat of vaporisation is 9710 cals./mole, and Trouton's constant is 24·1.

Fluorination of iso*Butyldipropylamine.*—The passage of 28·5 g. of this amine over cobalt trifluoride at 320°, followed by recycling at 300°, gave *perfluoroisobutyldipropylamine* (0·5 g.) (Found: C, 20·6; N, 2·6; F, 75·8. $C_{10}NF_{23}$ requires C, 21·0; N, 2·4; F, 76·5%), b. p. 146—148°, n_D^{25} 1·283(5); d_4^{25} 1·84(1).

Fluorination of Tributylamine.—Tributylamine (175 g. at 4 ml./hr.) was treated with cobalt trifluoride at 350° and gave *perfluorotributylamine* (5·8 g.) [Found: C, 21·2; N, 2·1; F, 76·0%; *M* (ebullioscopic), 663, 668. $C_{12}NF_{27}$ requires C, 21·45; N, 2·1; F, 76·45%; *M*, 671], b. p. 179·1—179·5°, n_D^{25} 1·291, n_D^{14} 1·296, d_4^{25} 1·873.

Chemical Properties of the Perfluoro-tert.-*amines.*—These compounds resemble nitrogen trifluoride and the fluorocarbons. They are stable, unreactive, and show no basic properties.

Physical Properties of the Perfluoro-tert.-*amines.*—The molecular refractions of these amines, calculated by the Lorentz–Lorenz expression from the data recorded above, are shown below:

Compound.	$N(C_2F_5)_3$.	$N(C_3F_7)_3$.	$N(C_3F_7)_3$(*iso*-C_4F_9).	$N(C_4F_9)_3$.
$[M]_D$	35·28	49·95	55·03	65·09
Atomic refraction (fluorine)	1·20	1·21	1·22	1·23

In the calculation of the atomic refraction of fluorine, the atomic refraction of nitrogen was taken as 2·74, the value derived by Vogel ("Practical Organic Chemistry," Longmans Green and Co., London, 1948, p. 898) for tertiary amines, and the atomic refraction of carbon as 2·418.

The molecular refractions of perfluoropiperidine and perfluoro*cyclo*hexylamine are 28·45 and 33·31 and the atomic refraction (fluorine) is 1·24 and 1·23(5). These values for the atomic refraction of fluorine are in agreement with those derived earlier for fluorocarbons.

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[*Received, August 12th*, 1950.]

23. αγ-*Diaminobutyric Acid.*

By S. WILKINSON.

αγ-Diaminobutyric acid has certain properties distinct from those of the higher homologues, ornithine and lysine: (*a*) this diamino-acid forms three characteristic hydrochlorides, (*b*) treatment of αγ-dicarbobenzyloxyaminobutyric acid with phosphorus pentachloride gives 1-carbobenzyloxy-3-(carbobenzyloxyamino)pyrrolid-2-one and not γ-(carbobenzyloxyamino)-α-carboxyaminobutyric acid anhydride, which one might expect by analogy with ornithine and lysine.

OUR present interest in αγ-diaminobutyric acid arises from its presence in acid hydrolysates of the antibiotic polypeptides, the polymyxins, from which both the DL-form (Catch and Jones, *Biochem. J.*, 1948, **42**, lii) and the L-form (Catch, Jones, and Wilkinson, *Ann. N.Y. Acad. Sci.*, 1949, **51**, 917) have been isolated. We now report some reactions of αγ-diaminobutyric acid which differ from those of the higher homologues, ornithine and lysine.

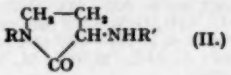
It was found that αγ-diaminobutyric acid gave not only the expected mono- and di-hydrochlorides, but also formed a third, stable hydrochloride of characteristic crystalline form, in which the amino-acid and hydrogen chloride were present in the molecular ratio, 2 : 3. This corresponds to Synge's observations (*Biochem. J.*, 1939, **33**, 671) that αγ-diaminobutyric acid forms three crystalline oxalates in which the proportions of oxalic acid are 0·5, 1·0, and 1·5 moles to each mole of amino-acid, whilst Carter, Abeele, and Rothrock's findings (*J. Biol. Chem.*, 1949, **178**, 325) that DL-αγ-diaminobutyric acid dihydrochloride, on repeated crystallisation from alcohol–water, was converted into the monohydrochloride, confirm, in part, our experiments.

The polypeptide structure of the polymyxins, and the presence of a new, naturally-occurring amino-acid, stimulated attempts to prepare polypeptides containing αγ-diaminobutyric acid residues. It was intended to polymerise γ-(carbobenzyloxyamino)-α-carboxyaminobutyric acid anhydride following the procedures described for the preparation of polylysine (Katchalski, Grossfeld, and Frankel, *J. Amer. Chem. Soc.*, 1947, **69**, 2565; 1948, **70**, 2095) and polyornithine (Katchalski and Spitnik, *Nature*, 1949, **164**, 1092).

Following the method for the synthesis of ε-carbobenzyloxy-α-carboxy-L-lysine anhydride (Bergmann, Zervas, and Ross, *J. Biol. Chem.*, 1935, **111**, 245), L-αγ-diaminobutyric acid (I) was converted into the dicarbobenzyloxy-derivative and treated in cold ethereal solution with

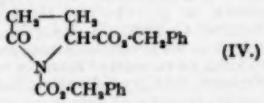
phosphorus pentachloride. On storage, a crystalline, optically active solid separated. This was apparently not the required anhydride but 1-carbobenzyloxy-3-(carbobenzyloxyamino)-

(I.) $CH_2 \cdot CH_2 \cdot CH \cdot CO_2H$ (NH_2, NH_2)

(II.) 

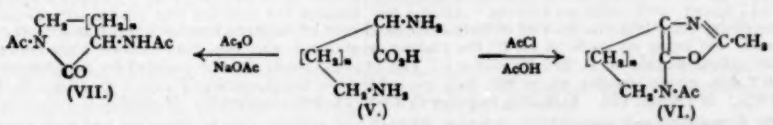
pyrrolid-2-one (II; R = R′ = $CO_2 \cdot CH_2Ph$). Hydrogenation of the product in ethanol in the presence of platinum oxide gave a product to which the 3-carbobenzyloxyamino-structure (II; R = H, R′ = $CO_2 \cdot CH_2Ph$) rather than the 1-carbobenzyloxyamino-structure (II; R = $CO_2 \cdot CH_2Ph$, R′ = H) was assigned, because of its inability to react with acetic anhydride and of the non-production of colour with ninhydrin. Both (II; R = R′ = $CO_2 \cdot CH_2Ph$) and (II; R = H, R′ = $CO_2 \cdot CH_2Ph$) were hydrogenated in glacial acetic acid in the presence of platinum oxide to 3-aminopyrrolid-2-one (II; R = R′ = H), which was isolated as a crystalline solid, m. p. 98—99°, by sublimation *in vacuo*. The product was optically active ($[\alpha]_D^{21}$ = −64·4° in water), gave a strong purplish-blue with ninhydrin, and was readily hydrolysed by hydrochloric acid to L-αγ-diaminobutyric acid. 3-Aminopyrrolid-2-one gave a picrate, m. p. 180—184°, and a mono-acetyl derivative, m. p. 191°, $[\alpha]_D^{21}$ = −97·3° in water. These physical constants were obviously different from those recorded by Adamson (*J.*, 1943, 39); the explanation was found in the partial racemisation which occurred under the relatively drastic condition employed by Adamson [cf. the racemisation when 2-ketopyrrolidine-4-carboxylic acid is prepared by heating glutamic acid (Arnew and Opsahl, *J. Biol. Chem.*, 1940, **134**, 649)]. L-αγ-Diaminobutyric acid was therefore converted into the ethyl ester dihydrochloride by Akabori and Numano's method (*Bull. Chem. Soc. Japan*, 1936, **11**, 214). The free ester on liberation in the cold cyclised on being kept, even at room temperature to give L-3-amino-pyrrolid-2-one, identical with that obtained by hydrogenation of the dicarbobenzyloxy-pyrrolidone (II; R = R′ = $CO_2 \cdot CH_2Ph$). Further proof of identity was shown by its conversion into L-3-acetamidopyrrolid-2-one, m. p. 191°, $[\alpha]_D^{21}$ = −97·3° in water. The ease of racemisation of L-3-aminopyrrolid-2-one was shown by heating a sample in a sealed tube at 155—160° for five hours (shorter times of heating caused only partial racemisation), whereupon DL-3-amino-pyrrolid-2-one was isolated; this gave DL-3-acetamidopyrrolid-2-one, hydrolysed by hydrochloric acid to DL-αγ-diaminobutyric acid. On the paper chromatogram the behaviour of DL- and L-3-aminopyrrolid-2-one was identical.

The course of the cyclisation of αγ-di(carbobenzyloxyamino)butyric acid has an analogy in Berenbom and White's observation (*J. Amer. Chem. Soc.*, 1949, **71**, 2246) that, unless the phosphorus oxychloride formed during the conversion of α-benzyl hydrogen *N*-carbobenzyl-

(III.) $CO_2 \cdot CH_2Ph$, $CH \cdot NH \cdot CO_2 \cdot CH_2Ph$, $CH_2 \cdot CH_2 \cdot COCl$ —$POCl_3$, NH_3→  (IV.)

oxyglutamate into the acid chloride (III) was removed, treatment of (III) with ammonia did not give the desired amide but intramolecular cyclisation occurred to give 1 : 5-dicarbo-benzyloxypyrrolid-2-one (IV).

The ease of cyclisation of ethyl αγ-diaminobutyrate led to an investigation of the cyclisation of the acid itself. When L-αγ-diaminobutyric acid (V; *n* = 1) monohydrochloride, acetic anhydride, and anhydrous sodium acetate were heated on the steam-bath racemisation occurred and from the reaction mixture DL-1-acetyl-3-acetamidopyrrolid-2-one (VII; *n* = 1) was isolated.



This is in contrast to Wrede's observation (*Z. physiol. Chem.*, 1932, **206**, 146) that treatment of lysine (V; *n* = 3) or ornithine (V; *n* = 2) with acetyl chloride and acetic acid at 100° caused racemisation and gave a compound, formulated as (VI; *n* = 3) or (VI; *n* = 2), respectively.

Experimental.

Hydrochlorides of αγ-Diaminobutyric Acid.—The *dihydrochlorides* were prepared by recrystallisation from concentrated hydrochloric acid or glacial acetic acid–concentrated hydrochloric acid. The DL-salt, m. p. 202—205° (decomp.), was isolated as beautiful hexagonal prisms (Found: N, 14·6; Cl, 37·1. $C_4H_{10}O_2N_2.2HCl$ requires N, 14·7; Cl, 37·2%), whilst the L-form gave unsymmetrical quadrilateral prisms, m. p. 197—198° (decomp.), $[\alpha]_D^{21}$ +13·3° (*c* = 0·25 in water), $[\alpha]_{5461}^{21}$ +16·2° (*c* = 0·8 in water) (Found: C, 25·2; H, 6·3; N, 14·5; Cl, 37·2. $C_4H_{10}O_2N_2.2HCl$ requires C, 25·1; H, 6·3; N, 14·7; Cl, 37·2%).

On careful crystallisation of the dihydrochlorides from aqueous alcohol, the respective *sesquihydrochlorides* were obtained in rosettes of slender prisms. The sesquihydrochlorides were also obtained on drying the dihydrochlorides *in vacuo* at 100°. The DL-salt had m. p. 194—196° (decomp.) (Found: N, 16·4; Cl, 30·5. $C_4H_{10}O_2N_2.1\frac{1}{2}HCl$ requires N, 16·2; Cl, 30·8%); the L-form had m. p. 211—212° (decomp.), $[\alpha]_D^{21}$ +13·5° (*c* = 0·8 in water), $[\alpha]_{5461}^{21}$ +16·2° (*c* = 0·8 in water), $[\alpha]_{5461}^{21}$ +26·9° (*c* = 0·8 in 5N-hydrochloric acid) (Found: C, 27·8; H, 6·4; N, 15·9; Cl, 30·8. $C_4H_{10}O_2N_2.1\frac{1}{2}HCl$ requires C, 27·8; H, 6·6; N, 16·2; Cl, 30·8%).

The *monohydrochlorides* were prepared from the dihydrochlorides on treatment with pyridine in aqueous alcohol. Recrystallisation from aqueous alcohol gave shallow rectangular prisms: DL-form, m. p. 229° (decomp.) (Found: C, 31·3; H, 7·0; N, 17·9; Cl, 22·7. $C_4H_{10}O_2N_2.HCl$ requires C, 31·1; H, 7·1; N, 18·1; Cl, 23·0%); L-form, m. p. 225° (decomp.), $[\alpha]_D^{21}$ +23·8° (*c* = 1·2 in 6N-hydrochloric acid), $[\alpha]_{5461}^{21}$ +28·6° (*c* = 1·2 in water), $[\alpha]_{5461}^{21}$ +10·0° (*c* = 1·7 in N-KOH) (Found: N, 18·2; Cl, 23·0); D-form, m. p. 223—224°, $[\alpha]_D^{21}$ −11·4° (*c* = 0·25 in water) (Found: N, 18·0; Cl, 22·8%).

Dipicrates of αγ-Diaminobutyric Acid.—The *dipicrates* were isolated as yellow, long fine prisms by crystallisation from water: DL-form, m. p. 189° (decomp.) (Found: C, 33·1; H, 2·5; N, 19·5. $C_4H_{10}O_2N_2.2C_6H_3O_7N_3$ requires C, 33·3; H, 2·8; N, 19·5%); L-form, m. p. 187° (decomp.) (Found: C, 33·7; H, 2·6; N, 19·5%); D-form, m. p. 187° (Found: N, 19·6%).

The D-glutamic acid used in the synthesis of D-αγ-diaminobutyric acid was prepared by hydrolysis of the D-glutamylpeptide from the capsule of *Bacillus anthracis* (cf. Bruckner and Ivanovics, *Z. physiol. Chem.*, 1937, **247**, 281).

L-*αγ-Di(carbobenzyloxyamino)butyric Acid.*—To a solution of L-αγ-diaminobutyric acid monohydrochloride (18·9 g.) in sodium hydroxide solution (122·4 ml.; 2N.) maintained at 0°, benzyl chloroformate (41·7 g.) and sodium hydroxide solution (183·6 ml.; 2N.) were added in four equal portions at intervals of thirty minutes and with vigorous stirring. After being stirred for a further two hours the mixture was acidified with hydrochloric acid and extracted with chloroform. The chloroform solution was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in micro-needles, m. p. 91—92° (33 g.) (Found: C, 62·2; H, 5·7; N, 7·2. $C_{20}H_{22}O_6N_2$ requires C, 62·2; H, 5·7; N, 7·25%). The acid was insoluble in water, readily soluble in alcohol, somewhat soluble in ether, and did not produce any characteristic colour with ninhydrin.

L-1-*Carbobenzyloxy*-3-(*carbobenzyloxyamino*)*pyrrolid*-2-*one.*—αγ-Di(carbobenzyloxyamino)butyric acid (73·9 g.) was dissolved in dry ether (500 ml.), cooled to −5° and phosphorus pentachloride (44 g.) added, with stirring. After a further twenty minutes a clear solution was obtained and then on more prolonged cooling a crystalline mass separated, which was filtered off and washed several times with cold ether. Recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°) or ethyl acetate–ether gave prisms, m. p. 113—114° (45 g.) [Found: C, 65·2; H, 5·3; N, 7·7%; *M* (Rast), 358. $C_{20}H_{20}O_5N_2$ requires C, 65·2; H, 5·4; N, 7·6%; *M*, 350]. The *pyrrolidone* was optically active, $[\alpha]_{5461}^{21}$ = −35·1° (*c* = 0·8 in ethyl acetate), and did not produce any characteristic colour with ninhydrin. A further crop (12 g.) was isolated from the original ether solution by concentration *in vacuo*, trituration with light petroleum, and crystallisation from ethyl acetate–ether.

Ethyl L-*αγ-Diaminobutyrate Dihydrochloride.*—L-αγ-Diaminobutyric acid monohydrochloride (35 g.) was suspended in dry absolute ethanol (1000 ml.) and dry hydrogen chloride passed into the boiling mixture until a clear solution was obtained. The solution was refluxed for 6 hours and concentrated to dryness *in vacuo*, and any residual hydrochloric acid removed by reconcentration *in vacuo* after the addition of ethanol and then benzene. The resinous mass slowly crystallised after prolonged drying in a vacuum desiccator over phosphoric oxide and was twice recrystallised, first from ethanol–benzene and then from ethanol–ether, giving prisms, m. p. 172° (decomp.) (29 g.), very soluble in water and ethanol and somewhat hygroscopic (Found: N, 12·6. $C_6H_{14}O_2N_2Cl_2$ requires N, 12·7%). The product gave a purplish-blue colour with ninhydrin.

L-3-*Aminopyrrolid*-2-*one.*—The ester dihydrochloride (28 g.) was dissolved in absolute ethanol (100 ml.), cooled to −5°, and a solution of sodium ethoxide [from sodium (5·9 g.)] in absolute alcohol (100 ml.) added, with vigorous stirring. After a few minutes the mixture was diluted with twice the volume of dry ether, the precipitated sodium chloride filtered off, and the filtrate concentrated to dryness *in vacuo*. On being set aside at *ca.* 0° the residue crystallised, and was recrystallised from benzene–acetone giving plates, m. p. 98—99° (18 g.). The product could also be purified by sublimation at 80°/10^{-2} mm. giving needles, m. p. 99°, $[\alpha]_D^{21}$ = −64° (*c* = 1·8 in water) [Found: C, 48·0; H, 7·9; N, 27·9%; *M* (Rast), 105. $C_4H_8ON_2$ requires C, 48·0; H, 8·0; N, 28·0%; *M*, 100].

The *pyrrolidone* was very soluble in water, ethanol, and acetone, very hygroscopic, and gave a strong purplish-blue colour with ninhydrin; it did not give the deep-red coloration characteristic of a diketopiperazine on being warmed with an alkaline solution of picric acid (Abderhalden, *Z. physiol. Chem.*, 1924, **139**, 181). Acetylation by means of acetic anhydride gave L-3-*acetamidopyrrolid*-2-*one*, crystallising from acetone in needles, m. p. 191°, $[\alpha]_D^{21}$ = −97·3° (*c* = 1·8 in water) [Found: C, 51·0; H, 7·0; N,

19·6%; *M* (Rast), 119. $C_4H_{10}O_2N_2$ requires C, 50·7; H, 7·0; N, 19·7%; *M*, 142]. The *hydrochloride*, precipitated when dry hydrogen chloride was passed through an alcoholic solution of the pyrrolidone, crystallised from ethanol–ether in needles, m. p. 186° (Found: C, 35·0; H, 6·6; N, 20·3; Cl, 25·9. $C_4H_9ON_2Cl$ requires C, 35·2; H, 6·6; N, 20·5; Cl, 26·0%). The *hydrogen oxalate* crystallised from moist alcohol in needles, softening at 120° and decomposing vigorously at 140° (Found: N, 14·8. $C_8H_{12}O_6N_2$ requires N, 14·7%). The *picrate* crystallised from aqueous alcohol in yellow prisms, m. p. 180—184° (decomp.) after darkening, softening at 170° (Found: C, 36·8; H, 3·4; N, 21·0. $C_{10}H_{11}O_9N_5$ requires C, 36·48; H, 3·3; N, 21·3%).

Hydrolysis with 6N-hydrochloric acid gave L-αγ-diaminobutyric acid, which was isolated as its monohydrochloride, m. p. 225° (decomp.), $[\alpha]_{5461}^{21} = +27·0°$ ($c = 2·6$ in N-hydrochloric acid), and also identified by conversion into the dipicrate, which crystallised from water in yellow prisms, m. p. 187° (decomp.).

L-3-(*Carbobenzyloxyamino*)*pyrrolid*-2-*one*.—L-1-Carbobenzyloxy-3-(carbobenzyloxyamino)pyrrolid-2-one (2·6 g.) was dissolved in absolute alcohol (60 ml.) and hydrogenated in the presence of Adams's catalyst (0·8 g.). After the adsorption of 1 mol. of hydrogen the rate of hydrogenation was negligible. The catalyst was filtered off and, after evaporation of the alcohol *in vacuo*, the residue crystallised from ethanol–light petroleum (b. p. 60—80°) as plates, m. p. 178° (1·9 g.), $[\alpha]_{5461}^{21} = -52·3°$ ($c = 0·9$ in ethanol). (Alternatively the alcohol solution was concentrated *in vacuo* and the solid residue extracted with warm water, and filtered. When the filtrate was cooled a crystalline mass of L-3-(*carbobenzyloxyamino*)-*pyrrolid*-2-*one* separated.) [Found: C, 61·3; H, 5·9; N, 11·9%; *M* (Rast), 270. $C_{13}H_{14}O_3N_2$ requires C, 61·55; H, 6·0; N, 12·0%; *M*, 234]. The product was sparingly soluble in cold water but readily soluble in hot water; it did not produce any characteristic colour with ninhydrin.

The product was warmed on the steam-bath for 15 minutes with acetic anhydride; the mixture was concentrated to dryness *in vacuo* and the residue crystallised from acetone giving plates, m. p. 177° (undepressed on admixture with the starting material).

L-3-*Aminopyrrolidone*.—(a) *By catalytic hydrogenation of* L-1-*carbobenzyloxy*-3-(*carbobenzyloxyamino*)-*pyrrolid*-2-*one in glacial acetic acid*. The dicarbobenzyloxypyrrolidone (2·85 g.) was hydrogenated in glacial acetic acid (50 ml.) in the presence of platinum oxide (1 g.). After the absorption of 2 mols. of hydrogen the reaction ceased. The catalyst was filtered off, the solvent removed *in vacuo*, the residue triturated several times with warm dry ether, and dried in a vacuum-desiccator over phosphoric oxide. A sample of the dried resinous material was dissolved in cold ethanol, and the solution made faintly alkaline with sodium methoxide and concentrated to dryness *in vacuo*. The residue was extracted with acetone and filtered, and the filtrate sublimed *in vacuo* at 90°/10^{-2} mm. to give a crystalline sublimate, m. p. 98—99° not depressed on admixture with L-3-aminopyrrolid-2-one prepared as described previously (Found: N, 28·0. Calc. for $C_4H_8ON_2$: N, 28·0%). The product was optically active, $[\alpha]_D^{21} = -64·4°$ ($c = 1·8$ in water), and gave a purplish-blue colour with ninhydrin but none with alkaline sodium picrate.

The hydrochloride crystallised from ethanol–ether in needles, m. p. 186° (undepressed on admixture with the pyrrolidone hydrochloride obtained previously) (Found: C, 35·2; H, 6·5. Calc. for $C_4H_9ON_2Cl$: C, 35·2; H, 6·6%). The hydrogen oxalate crystallised from ethanol in platelets which decomposed at 140° after softening at 120°.

The 2 : 4-*dinitrophenyl* derivative crystallised from aqueous alcohol in yellow needles, m. p. 205—206° (not depressed on admixture with a sample prepared from the 3-aminopyrrolidone obtained previously) (Found: N, 18·8. $C_{10}H_{11}N_4O_7$ requires N, 18·7%).

The resin (0·6 g.) was gently warmed for a few minutes with acetic anhydride (2 ml.); the solution was cooled and diluted with ether, and the crystalline precipitate was filtered off and crystallised from acetone giving L-3-acetamidopyrrolidone (0·6 g.) as plates, m. p. 192° (alone or on admixture with the previous sample), $[\alpha]_D^{21} = -96·5°$ ($c = 0·8$ in water) (Found: C, 51·0; H, 6·9; N, 20·0. Calc. for $C_6H_{10}O_2N_2$: C, 50·7; H, 7·0; N, 19·7%). The product may also be purified by sublimation at 140°/10^{-2} mm.

The resin (0·5 g.) was also heated on the steam-bath for 30 minutes with hydrochloric acid (25 ml.; 6N.). After being concentrated *in vacuo*, the residue was dried and dissolved in alcohol, and pyridine slowly added. The precipitate was filtered off and recrystallised from moist alcohol to give L-αγ-diaminobutyric acid monohydrochloride, m. p. 225° (decomp.), $[\alpha]_{5461}^{21} = +26·8°$ ($c = 2·5$ in N-hydrochloric acid).

(b) *By catalytic hydrogenation of* L-3-(*carbobenzyloxyamino*)*pyrrolid*-2-*one in glacial acetic acid*. L-3-(Carbobenzyloxyamino)pyrrolid-2-one (0·15 g.) in glacial acetic acid (15 ml.) was hydrogenated in the presence of platinum oxide (0·13 g.); after the absorption of 1 mol. of hydrogen, the reaction ceased. The catalyst was filtered off and the solvent removed *in vacuo*. The residual resin, after treatment as described above, was sublimed at 80—90°/10^{-2} mm. to yield a crystalline sublimate, m. p. 98° (0·08 g.).

L-3-Acetamidopyrrolidone, prepared in the usual manner, was isolated as plates, m. p. 191—192°, $[\alpha]_D^{21} = -96°$ ($c = 1$ in water).

The resin was distilled from a small distillation flask, and had b. p. 120—130°/10^{-2} (oil-bath at 160—180°). The main bulk rapidly darkened in colour but a clear distillate (*ca.* 50%) was obtained which set to a crystalline mass, m. p. *ca.* 98—100°, $[\alpha]_D^{21} = -27°$ ($c = 0·7$ in water).

The partially racemised *acetyl* derivative, prepared from the above distillate, crystallised from acetone in needles, m. p. 176—177° (after some preliminary softening at 172°), $[\alpha]_D^{21} = -62·0°$ ($c = 0·64$ in water) [Found: C, 50·9; H, 6·8; N, 20·1%; *M* (Rast), 117. $C_6H_{10}O_2N_2$ requires C, 50·7; H, 7·0; N, 19·7%; *M*, 142]. Hydrolysis with 6N-hydrochloric acid gave a partially racemised L-αγ-diaminobutyric acid monohydrochloride, $[\alpha]_{5461}^{21} = +21·8°$ ($c = 2·7$ in N-hydrochloric acid).

The *picrate* crystallised from aqueous alcohol in yellow needles, m. p. 198—200° (decomp.) (Found: C, 36·8; H, 3·1. $C_4H_8ON_2,C_6H_3O_7N_3$ requires C, 36·48; H, 3·3%).

The Racemisation of L-3-*Aminopyrrolidone.*—A sample of L-3-aminopyrrolidone (0·7 g.) was heated in a sealed tube in an atmosphere of nitrogen at 150° for 30 minutes, then at 170° for 15 minutes. The melt darkened and on cooling solidified; sublimation at 90/°10^{-3} mm. gave a crystalline solid (0·48 g.), m. p. 93—96° (after softening at 92°), $[\alpha]_D^{21} = -54{\cdot}7°$ ($c = 1{\cdot}8$ in water). The acetyl derivative, m. p. 177—178° (after softening at 168°), $[\alpha]_D^{21} = -59°$ ($c = 1{\cdot}1$ in water), on hydrolysis with 6N-hydrochloric acid gave a partially racemised L-α*γ*-diaminobutyric acid, $[\alpha]_{5461}^{21} = +21{\cdot}8°$ ($c = 2{\cdot}6$ in water).

A sample of L-3-aminopyrrolidone (0·8 g.) was heated in a sealed tube in an atmosphere of nitrogen for 5 hours at 155—160°. The resulting brown solid was sublimed at 100°/10^{-1} mm. to give DL-3-*aminopyrrolidone* (0·5 g.) [Found: N, 27·8%; *M* (Rast), 119. $C_4H_8ON_2$ requires N, 28·0%; *M*, 100].

DL-3-*Acetamidopyrrolidone*, prepared from the above, crystallised from acetone in needles, m. p. 174—175°, $[\alpha]_{5461}^{21} = 0{\cdot}00°$ ($c = 0{\cdot}8$ in water) [Found: C, 51·0; H, 7·0; N, 19·6%; *M* (Rast), 145. $C_6H_{10}O_2N_2$ requires C, 50·7; H, 7·0; N, 19·7%; *M*, 142]. Hydrolysis of the DL-3-acetamidopyrrolidone with 6N-hydrochloric acid gave DL-α*γ*-diaminobutyric acid monohydrochloride, m. p. 228—229° (decomp.), $[\alpha]_{5461}^{21} = 0{\cdot}00°$ ($c = 1{\cdot}2$ in N-hydrochloric acid).

DL-3-*Acetamido*-1-*acetylpyrrolidone*. L-α*γ*-Diaminobutyric acid monohydrochloride (4 g.) was heated on the steam-bath for 3 hours with acetic anhydride (25 ml.) and anhydrous sodium acetate (1 g.). The mixture was cooled, filtered, and concentrated to dryness *in vacuo*. The residue was extracted with hot acetone, and the solution filtered from the insoluble solid and concentrated *in vacuo*. The residual resin crystallised from acetone–ether in rosettes of prisms (2·8 g.), m. p. 132°, $[\alpha]_{5461}^{21} = 0{\cdot}00°$ ($c = 1{\cdot}3$ in water) [Found: C, 52·2; H, 6·6; N, 15·3%; *M* (Rast), 220. $C_8H_{12}O_2N_2$ requires C, 52·2; H, 6·5; N, 15·2%; *M*, 184]. The product was readily soluble in water and did not give any characteristic colour with ninhydrin.

Distillation in a micro-molecular still gave a clear resin, b. p. 120°/10^{-3} mm., which set to a hard crystalline mass on being kept.

The author thanks Dr. Tudor S. G. Jones for his co-operation in carrying out the chromatographic work, Mr. A. Bennett for the analytical results, Dr. J. R. Catch with whom some of the earlier results were obtained, and Dr. D. W. Adamson for his continued interest and advice.

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[*Received, September 12th*, 1950.]

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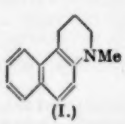
24. *A New Technique for the Reduction of Certain Heterocyclic Methiodides.*

By J. A. BARLTROP and D. A. H. TAYLOR.

A convenient method, which is adaptable to large-scale operations, has been developed for the preparation of both simple and polynuclear 1-alkylpiperidine derivatives. It involves the hydrogenation of a quaternary salt of the pyridine over Raney nickel catalyst in the presence of a base, such as diethylamine. The corresponding *N*-methylpiperidines and tetrahydro-*N*-methyl-quinolines and -*iso*quinolines are readily obtained in excellent yield. The methosulphates are not suitable substrates because further methylation of the reduced compound occurs.

DURING the course of other investigations, it became necessary to prepare on a relatively large scale 1 : 2 : 3 : 4-tetrahydro-1-methyl-5 : 6-benzoquinoline (I). The methylation of 1 : 2 : 3 : 4-tetrahydro-5 : 6-benzoquinoline by formaldehyde and formic acid gave a somewhat impure specimen of (I) in 26% yield, whilst use of methyl iodide and potassium carbonate in acetone gave only 39% of the required product. In the hope of improving these yields we examined the reduction of 5 : 6-benzoquinoline methiodide.



(I.)

The standard techniques for reductions of this type leave much to be desired. Hydrogenation of heterocyclic methiodides over platinum oxide, because of the expense of the catalyst and the necessity of using it in relatively high concentrations, is, in general, limited to small-scale runs only. Reduction by dissolving metals, *e.g.* tin and hydrochloric acid or sodium and ethanol, gives yields that are variable and often poor, and the isolation of the product is frequently tedious. For these reasons, we decided to investigate the hydrogenation over Raney nickel catalyst, of heterocyclic methiodides in general, and 5 : 6-benzoquinoline methiodide in particular.

As a trial experiment, quinoline methiodide was hydrogenated, alone, in the presence of Raney nickel. From the resulting complex mixture, which contained free iodine, a substance which appeared to be *cis*-decahydro-1-methylquinoline was isolated in 17% yield. Since it appeared likely that the hydrogen iodide liberated in the course of the reduction, was interfering, a second hydrogenation was performed under identical conditions of temperature and pressure in the presence of 1 equivalent of potassium hydroxide. This led to the formation of 1 : 2 : 3 : 4-tetrahydro-1-methylquinoline in 54% yield. It seemed possible that the factor limiting the yield obtained in this experiment was the instability of the pseudo-base, formed by the interaction of the quaternary salt and the alkali. In order to minimise this effect, the potassium hydroxide was replaced by diethylamine. This modification was completely successful, tetrahydro-1-methylquinoline being obtained in over 90% yield.

This technique, when applied to the hydrogenation of 5 : 6-benzoquinoline methiodide, gave 1 : 2 : 3 : 4-tetrahydro-1-methyl-5 : 6-benzoquinoline (I) in 90% yield. In order to determine the scope of this process, the methiodides of a number of pyridines, quinolines, and *iso*quinolines were subjected to hydrogenation under similar conditions. The corresponding 1-methylpiperidines and tetrahydro-*N*-methyl-quinolines and *-iso*quinolines were obtained in yields varying between 78 and 95%. The lower yields associated with the piperidines are caused by mechanical losses consequent upon their extreme solubility in water.

Other secondary amines, such as piperidine, can be used in place of diethylamine with equal success, but the heterocyclic methosulphates appear to be unsuitable because the reduced compound is further methylated by the methosulphate anion at the high temperatures involved.

Experimental.

1 : 2 : 3 : 4-*Tetrahydro*-1-*methyl*-5 : 6-*benzoquinoline*.—(*a*) 1 : 2 : 3 : 4-Tetrahydro-5 : 6-benzoquinoline (10·8 g.) and formaldehyde (4·4 c.c.; 40%) were heated on the steam-bath and formic acid (8·8 c.c.; 85%) was added during 15 minutes. After being heated for 6 hours, the red mass was treated with concentrated hydrochloric acid (6 c.c.), and the whole evaporated to dryness *in vacuo*. The residue was dissolved in water, decolorised with charcoal, and basified, and the product isolated with ether and distilled. The *base* (3 g.) was collected at 212°/12 mm. as an oil, slowly setting to pearly flakes, m. p. 61°. The *picrate* crystallised from ethanol in yellow needles, m. p. 163° (Found : C, 56·5; H, 4·3. $C_{14}H_{15}N,C_6H_3O_7N_3$ requires C, 56·3; H, 4·2%).

(*b*) The tetrahydro-5 : 6-benzoquinoline (9 g.) in acetone (50 c.c.) was boiled under reflux with methyl iodide (7·5 g.) and potassium carbonate (16·5 g.) for 15 hours. The filtered solution, on evaporation, deposited an oil and a crystalline solid, which proved to be the *methiodide* of 1 : 2 : 3 : 4-tetrahydro-1-methyl-5 : 6-benzoquinoline. The oil, separated by solution in ether, was distilled; the tetrahydro-1-methyl-5 : 6-benzoquinoline (3·9 g.) was collected at 210°/10 mm. and was identified by means of its picrate, m. p. and mixed m. p. 163°. The methiodide crystallised from water in needles, m. p. 187° (Found : C, 51·9; H, 5·3; N, 3·9. $C_{15}H_{18}NI,\frac{1}{2}H_2O$ requires C, 51·7; H, 5·5; N, 4·0%).

(*c*) 5 : 6-Benzoquinoline methiodide (25 g.), suspended in a mixture of ethanol (100 c.c.) and diethylamine (15 c.c.), was hydrogenated over Raney nickel catalyst at 180° and 75 atmospheres for 2 hours. The solution, filtered from catalyst, was distilled. The tetrahydro-1-methyl-5 : 6-benzoquinoline (11·8 g., 90%), m. p. and mixed m. p. 61°, was collected at 210°/10 mm. (Found : C, 85·3; H, 7·5; N, 7·1. $C_{14}H_{15}N$ requires C, 85·2; H, 7·6; N, 7·1%).

Hydrogenation of Quinoline Methiodide.—(*a*) Quinoline methiodide (13·6 g.), dissolved in ethanol (100 c.c.), was hydrogenated over Raney nickel catalyst at 135° and 75 atmospheres. After the catalyst had been removed by filtration, and the filtrate evaporated, a red oil was obtained which contained iodine. Distillation gave what appeared to be *cis*-decahydro-1-methylquinoline (1·3 g., 17%), b. p. 80°/15 mm. This gave a picrate, m. p. 199—200° (Found : C, 50·0; H, 5·5. Calc. for $C_{10}H_{19}N,C_6H_3O_7N_3$: C, 50·3; H, 5·8%). Ehrenstein and Bunge (*Ber.*, 1934, **67**, 1715) record m. p. 199—200°.

(*b*) Quinoline methiodide (13·6 g., 0·05 mol.), dissolved in ethanol (100 c.c.), was treated with potassium hydroxide (2·8 g., 0·05 mol.) and hydrogenated over Raney nickel catalyst under conditions identical with those described in (*a*). The filtered solution was evaporated and the product isolated with ether and distilled. 1 : 2 : 3 : 4-Tetrahydro-1-methylquinoline (4 g., 54%) was collected at 120°/15 mm. It was identified by m. p. and mixed m. p. of the picrate and methiodide.

(*c*) A solution of quinoline methiodide (30 g.) in ethanol (400 c.c.) was treated with diethylamine (25 c.c.) and hydrogenated over Raney nickel catalyst at 140° and 60 atmospheres. After the product had been worked up in the usual manner, 1 : 2 : 3 : 4-tetrahydro-1-methylquinoline (15 g., 94%), b. p. 115°/10 mm., was obtained. The picrate separated from ethanol in yellow needles, m. p. 125° alone, and when mixed with an authentic specimen (*lit.*, m. p. 125°).

1-*Methylpiperidine*.—Pyridine methiodide (38 g.), dissolved in ethanol, was treated with diethylamine (25 c.c.) and hydrogenated over Raney nickel catalyst for 3 hours at 140° and 75 atmospheres. The filtered solution was acidified, evaporated to dryness, and basified strongly, and the product isolated with ether. Fractionation over potassium hydroxide gave 1-methylpiperidine (13 g., 78%), b. p. 107° (Found : C, 72·6; H, 13·2. Calc. for $C_6H_{13}N$: C, 72·7; H, 13·1%). The picrate, m. p. 218°, formed yellow needles from ethanol (Found : C, 44·2; H, 5·1. Calc. for $C_6H_{13}N,C_6H_3O_7N_3$: C, 43·9; H, 4·9%).

1-*Methyl-α-pipecoline.*—α-Picoline methiodide (40 g.) dissolved in ethanol (400 c.c.) was treated with diethylamine (25 c.c.) and hydrogenated under the same conditions as those of the preceding experiment; 1-methyl-α-pipecoline (15·5 g., 80%), b. p. 118°, was obtained (Found: C, 74·2; H, 13·7. Calc. for $C_7H_{15}N$: C, 74·3; H, 13·3%). The picrate separated from ethanol in yellow needles, m. p. 134° (*lit.*, m. p. 134°).

1 : 2 : 3 : 4-*Tetrahydro-2-methylisoquinoline.*—*iso*Quinoline methiodide (8 g.), ethanol (120 c.c.), and diethylamine (5 c.c.) were hydrogenated for 2 hours at 180° and 75 atmospheres. Tetrahydro-2-methyl-*iso*quinoline (3·7 g., 86%), b. p. 123°/35 mm., was isolated. The methiodide separated from ethanol in prisms, m. p. 189° (Found: C, 45·9; H, 5·4. Calc. for $C_{11}H_{16}NI$: C, 45·7; H, 5·5%) (*lit.*, m. p. 189°).

1 : 2 : 3 : 4-*Tetrahydro*-1 : 6 : 8-*trimethylquinoline.*—6 : 8-Dimethylquinoline (3 g.) and methyl iodide (2 c.c.) were heated in a sealed tube for 1 hour at 100°. The methiodide (3 g.), dissolved in ethanol (100 c.c.), was hydrogenated in the presence of diethylamine (5 c.c.) for 2 hours at 140° and 75 atmospheres. 1 : 2 : 3 : 4-Tetrahydro-1 : 6 : 8-trimethylquinoline (1·5 g., 86%), b. p. 127°/15 mm., was obtained as an oil, which set to a solid, m. p. 48°. The mixed m. p. with an authentic specimen, prepared by Mr. S. L. Cosgrove (D. Phil. Thesis, Oxford, 1950), was 48°.

(±)-*Laudanosine.*—Papaverine methiodide (4·25 g.), dissolved in ethanol (100 c.c.), was treated with diethylamine (5 c.c.) and hydrogenated over Raney nickel catalyst for 3 hours at 180° and 60 atmospheres. The filtered solution was evaporated to dryness. The residual (±)-laudanosine, when crystallised from ethanol, formed fine needles (3 g., 95%), m. p. 114° alone and when mixed with an authentic specimen.

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, September 14th*, 1950.]

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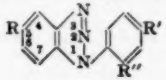
25. *Experiments on the Preparation of Indolocarbazoles. Part II. Some Observations on the Graebe–Ullmann Carbazole Synthesis.*

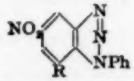
By G. G. COKER, S. G. P. PLANT, and P. B. TURNER.

3- and 1-Chloro-6-nitro-, 1-chloro-3-nitro-, 6-cyano-3-methyl-, 6-cyano-1-methyl-, 3- and 1-chloro-6-cyano-, and 6-cyano-1-methyl-3-nitro-carbazole have been prepared by the Graebe–Ullmann reaction, but attempts to obtain carbazoles from certain other 5-nitro-1-phenylbenzotriazoles failed. The investigations have formed the basis for experiments designed to obtain indolocarbazoles from bistriazoles. Some structural problems in the polynitrodiphenylamines required as intermediates have been elucidated.

APPLICATIONS of the Graebe–Ullmann synthesis of carbazole derivatives (*Annalen*, 1896, **291**, 16) usually involve the preparation of a 2-nitrodiphenylamine and its conversion through the corresponding 2-amino-compound into a 1-phenylbenzotriazole, from which nitrogen is finally eliminated. Although the reactions have been applied to a number of compounds, information regarding the effect of different substituents in the various positions of the triazole molecule on the yield of the carbazole is still relatively meagre. During studies which are in progress in this laboratory into the synthesis and reactions of indolocarbazoles (*J.*, 1949, S 160 is regarded as Part I of this series) the possibility of applying the Graebe–Ullmann reaction to suitable bistriazoles as in the examples below is being investigated. The facile preparation of the requisite diphenylamines in most cases necessitates the condensation of a feebly-basic substituted



(I.)



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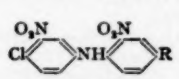


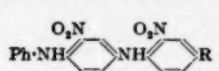
(III.)

aniline with an *o*-halogenonitrobenzene containing an additional activating substituent, such as nitro- or cyano- *para* to the halogen. Earlier attempts to prepare carbazoles from the simplest analogues of the corresponding triazoles have been mainly disappointing. Thus, although Preston, Tucker, and Cameron (*J.*, 1942, 500) obtained a 34% yield of 3-cyanocarbazole from the triazole (I; R = CN, R′ = R″ = H), only a trace of 3-nitrocarbazole resulted from (I; R = NO_2, R′ = R″ = H). Again, Blom (*Helv. Chim. Acta*, 1921, **4**, 1036) failed to obtain carbazoles from the triazoles (I; R = NO_2, R′ = Cl or EtO, R″ = H). It therefore seemed desirable to investigate more fully the application of the reaction to some simpler substances related to the intermediates in the projected indolocarbazole syntheses.

We have confirmed the observation that only a trace of 3-nitrocarbazole is formed in this

way, and have been unable to obtain the corresponding carbazoles from the closely related 5-nitro-1-*p*-tolyl- (I; R = NO_2, R′ = Me, R″ = H), 5-nitro-1-*o*-tolyl (I; R = NO_2, R′ = H, R″ = Me), 7-methyl-5-nitro-1-phenyl- (II; R = Me), 1-(2-methyl-4-nitrophenyl)-5-nitro- (I; R = R′ = NO_2, R″ = Me), and 1-(2-chloro-4-nitrophenyl)-5-nitro-benzotriazole (I; R = R′ = NO_2, R″ = Cl). Other 5-nitro-1-phenylbenzotriazoles have given better results, and the yields of the corresponding carbazoles shown in parentheses have been obtained from 1-*p*-chlorophenyl-5-nitro- (I; R = NO_2; R′ = Cl; R″ = H) (7%; contrast Blom's observation), 1-*o*-chlorophenyl-5-nitro- (I; R = NO_2; R′ = H; R″ = Cl) (14%), and 7-chloro-5-nitro-1-phenyl-benzotriazole (II; R = Cl) (28%). Evidently the presence of chlorine, unlike that of methyl, in the 7-, 1-*o*-, or 1-*p*-position facilitates the reaction in this group. As found by Preston, Tucker, and Cameron in the simplest case, the use of 5-cyano-1-phenylbenzotriazoles has given much more satisfactory products, and carbazoles have been prepared from 5-cyano-1-*p*-tolyl- (I; R = CN, R′ = Me, R″ = H) (57%), 5-cyano-1-*o*-tolyl- (I; R = CN, R′ = H, R″ = Me) (71%), 1-*p*-chlorophenyl-5-cyano- (I; R = CN, R′ = Cl, R″ = H) (22%), 1-*o*-chlorophenyl-5-cyano- (I; R = CN, R′ = H, R″ = Cl) (15%), and 5-cyano-1-(2-methyl-4-nitrophenyl)benzotriazole (I; R = CN, R′ = NO_2, R″ = Me) (8%). It is noteworthy, however, that in this series the presence of methyl rather than chlorine as a substituent in the 1-phenyl group leads to increased yields.

In first attempts to prepare substituted indolocarbazoles, 4-chloro-3-nitroaniline has been condensed with 1-chloro-2 : 4-dinitrobenzene and with 4-chloro-3-nitrobenzonitrile; the products (III; R = NO_2 or CN) condensed with aniline to give the anilinodiphenylamines (IV; R = NO_2 or CN), but efforts to reduce the former to a diamine which could be converted into a bistriazole failed. The latter, however, was transformed in this way into 5-(5-cyanobenzotriazol-1-yl)-1-phenylbenzotriazole (V), but attempts to effect a double Graebe–Ullmann change with the formation of a cyanoindolocarbazole were unsuccessful.



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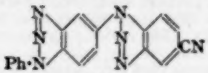

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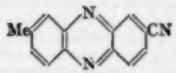

(VI.)

Some observations incidental to the preparation of the intermediates described in the Experimental section need comment. Reverdin and Crépieux (*Ber.*, 1903, **36**, 29; *Bull. Soc. chim.*, 1903, **29**, 235) heated 2-methyl-2′ : 4′-dinitrodiphenylamine with nitric acid (*d* 1·2) on a steam-bath for an hour and obtained a trinitro- (m. p. 158°) and a tetranitro-compound (m. p. 190°), but the structures were not determined. More satisfactory conditions have now been developed for the preparation of each of these substances, and the former has been shown to be 2-methyl-4 : 2′ : 4′-trinitrodiphenylamine by synthesis from 5-nitro-*o*-toluidine and 1-chloro-2 : 4-dinitrobenzene. The latter has also been obtained by the nitration of 2-methyl-4 : 6-dinitrodiphenylamine and so must be the 2-methyl-4 : 6 : 2′ : 4′-tetranitro-compound. The same authors were unable to isolate a pure substance from the nitration of the isomeric 3-methyl-2′ : 4′-dinitrodiphenylamine under similar conditions. It has been found, however, that the action of concentrated nitric acid on this dinitro-compound in glacial acetic acid at room temperature leads to a mixture containing 3-methyl-4 : 2′ : 4′-trinitrodiphenylamine, also synthesised from 6-nitro-*m*-toluidine. More vigorous conditions gave 3-methyl-4 : 6 : 2′ : 4′-tetranitrodiphenylamine, the structure of which was established by its preparation from 3-methyl-4 : 6-dinitrodiphenylamine. The nitration of the last was modified to give 3-methyl-4 : 6 : 4′-trinitrodiphenylamine, also obtained from *p*-nitroaniline and 1-chloro-3-methyl-4 : 6-dinitrobenzene.

Nitro-groups were readily introduced into the 2- and the 6-position of 4′-cyano-4-methyl-2′-nitrodiphenylamine, the orientation being established by the preparation of the same substance by nitrating the product of condensing 4-methyl-2 : 6-dinitrophenyltoluene-*p*-sulphonate with *p*-aminobenzonitrile. The intermediate compound, 4′-cyano-4-methyl-2 : 2′-dinitrodiphenylamine, was more conveniently obtained synthetically from 3-nitro-*p*-toluidine and 4-chloro-3-nitrobenzonitrile and, when reduced with sodium sulphide under conditions used to obtain most of the 2-aminodiphenylamines described below, it gave 2-cyano-7-methylphenazine (VI). 7-Chloro-2-cyanophenazine was similarly obtained from the analogous 4-chloro-compound. The introduction of one nitro-group, in the 4-position, into the isomeric 4′-cyano-2-methyl-2′-nitrodiphenylamine proceeded readily, however, the identity of the product being confirmed by synthesis from 5-nitro-*o*-toluidine. Further nitration gave 4′-cyano-2-methyl-4 : 6 : 2′-trinitrodiphenylamine.

Reverdin and Crépieux (*loc. cit.*) stated that a product, m. p. 182—183°, obtained by nitrating 4-chloro-2′ : 4′-dinitrodiphenylamine is a tetranitro-compound, but they did not establish its structure and relied solely on a nitrogen analysis for its composition. It has now been proved that this substance is 4-chloro-2 : 2′ : 4′-trinitrodiphenylamine, identical with a sample prepared synthetically from 4-chloro-2-nitroaniline. The tetranitro-compound obtained on further nitration was found to melt at 215° and has been shown to have the additional substituent in the 6-position.

It has already been shown by Reverdin and Crépieux that mononitration of 2-chloro-2′ : 4′-dinitrodiphenylamine involves substitution at the 4-position by the fact that they obtained the same product by chlorinating the requisite trinitro-compound. Further nitration has now been found to give the expected 2-chloro-4 : 6 : 2′ : 4′-tetranitrodiphenylamine.

Experimental.

2-Methyl-4 : 2′ : 4′-trinitrodiphenylamine.—(*a*) After 2-methyl-2′ : 4′-dinitrodiphenylamine (2 g.) had been shaken with glacial acetic acid (30 c.c.) containing nitric acid (7 c.c.; *d* 1·42), and the mixture left at room temperature overnight, the solid was crystallised from aqueous acetic acid, and *2-methyl-4 : 2′ : 4′-trinitrodiphenylamine* obtained in orange prisms (1·2 g.), m. p. 159° (Found: C, 49·2; H, 3·2. $C_{13}H_{10}O_6N_4$ requires C, 49·1; H, 3·1%). (*b*) A mixture of 1-chloro-2 : 4-dinitrobenzene (2 g.), 5-nitro-*o*-toluidine (1·6 g.), and potassium carbonate (3 g.) was heated for 2 hours at 165°, and the product extracted with boiling glacial acetic acid (100 c.c.). The filtered solution was boiled with charcoal, again filtered, and poured into water, and the gummy material boiled with acetone (1 c.c.). When cold, the solid trinitro-compound (1·4 g.) was collected, recrystallised from acetic acid, and obtained in prisms, m. p. 159°, identical (mixed m. p.) with the substance described above.

1-(2-Methyl-4-nitrophenyl)-5-nitrobenzotriazole.—A mixture of the above trinitro-compound (15 g.) and alcohol (40 c.c.) was heated on the steam-bath in a 3-l. flask, crystalline sodium sulphide (21 g.) in water (20 c.c.) added, and the whole shaken. After the violent reaction had subsided, hot water was added, and the mixture boiled, and filtered while still hot. When the solid was extracted with hot acetone, and the extract boiled with charcoal and evaporated to small bulk, *2′-amino-2-methyl-4 : 4′-dinitrodiphenylamine* (5·5 g.), dark red needles, m. p. 229° (from dimethylaniline), separated (Found: C, 54·1; H, 4·1. $C_{13}H_{12}O_4N_4$ requires C, 54·2; H, 4·2%). The amine (1 g.) was dissolved in hot glacial acetic acid (15 c.c.) containing concentrated hydrochloric acid (1 c.c.), and, with stirring, the mixture was cooled and treated with concentrated aqueous sodium nitrite (0·5 g.). After dilution with water, the solid was crystallised from alcohol, and *1-(2-methyl-4-nitrophenyl)-5-nitrobenzotriazole* (1 g.) obtained in yellow prisms, m. p. 185° (Found: C, 52·2; H, 2·9. $C_{13}H_9O_4N_5$ requires C, 52·1; H, 3·0%).

Unless otherwise stated, the analogous 2-aminodiphenylamines and derived 1-phenylbenzotriazoles described below were prepared by methods similar to those given above.

2-Methyl-4 : 6 : 2′ : 4′-tetranitrodiphenylamine.—(*a*) 2-Methyl-2′ : 4′-dinitrodiphenylamine (2 g.) was heated on the steam-bath with glacial acetic acid (30 c.c.) and nitric acid (10 c.c.; *d* 1·42) until a straw-coloured solution was obtained (about ½ hour). When the solid which separated when the mixture was cooled and kept for a day was crystallised from acetic acid, *2-methyl-4 : 6 : 2′ : 4′-tetranitrodiphenylamine* was isolated in yellow needles (1·4 g.), m. p. 190° (Found: C, 42·9; H, 2·7. $C_{13}H_9O_8N_5$ requires C, 43·0; H, 2·5%). The same substance was obtained by similar treatment of 2-methyl-4 : 2′ : 4′-trinitrodiphenylamine. (*b*) After a mixture of 2-methyl-4 : 6-dinitrophenyl toluene-*p*-sulphonate (29 g.; Ullmann and Sané, *Ber.*, 1911, **44**, 3730) and aniline (30 g.) had been heated first near the b. p. for ½ hour and then on the steam-bath for an hour, red crystals separated overnight. The mixture was stirred with glacial acetic acid (60 c.c.), then diluted with water, and the solid crystallised from acetic acid, from which 2-methyl-4 : 6-dinitrodiphenylamine was obtained in orange-red prisms (15 g.), m. p. 169°, identical with a specimen prepared from 2-chloro-3 : 5-dinitrotoluene as described by Nietzki and Rehe (*Ber.*, 1892, **25**, 3005). After the product (1 g.) had been set aside for a short time at room temperature with nitric acid (15 c.c.; *d* 1·42), addition of water precipitated the tetranitro-compound, identical (mixed m. p.) with the substance described above.

7-Methyl-5-nitro-1-phenylbenzotriazole.—Prepared from 2-methyl-4 : 6-dinitrodiphenylamine through the requisite amine which was not completely purified, this substance crystallised from ethanol in yellow plates, m. p. 198° (Found: C, 61·2; H, 3·8. $C_{13}H_{10}O_2N_4$ requires C, 61·4; H, 3·9%).

5-Nitro-1-m-tolylbenzotriazole.—3-Methyl-2′ : 4′-dinitrodiphenylamine was converted into *2′-amino-3-methyl-4′-nitrodiphenylamine*, red plates (Found: C, 64·2; H, 5·5. $C_{13}H_{13}O_2N_3$ requires C, 64·2; H, 5·3%), m. p. 117° (from aqueous ethanol), and thence into *5-nitro-1-m-tolylbenzotriazole*, colourless plates, m. p. 151° (from ethanol) (Found: C, 61·4; H, 4·1. $C_{13}H_{10}O_2N_4$ requires C, 61·4; H, 3·9%).

3-Methyl-4 : 2′ : 4′-trinitrodiphenylamine.—After a mixture of 1-chloro-2 : 4-dinitrobenzene (5 g.), 6-nitro-*m*-toluidine (4 g.), and anhydrous sodium acetate (4 g.) had been heated for an hour at 190° and the product extracted with hot glacial acetic acid (100 c.c.), the filtered solution was poured into dilute hydrochloric acid, and *3-methyl-4 : 2′ : 4′-trinitrodiphenylamine*, red prisms (4 g.), m. p. 171—172° (from acetic acid), was precipitated (Found: C, 49·3; H, 3·5%). A mixture was obtained by leaving 3-methyl-2′ : 4′-dinitrodiphenylamine at room temperature with glacial acetic acid and nitric acid (*d* 1·42) for several hours, but adsorption of the product on alumina led to the isolation of some of the above trinitro-compound together with an isomeride, probably *3-methyl-6 : 2′ : 4′-trinitrodiphenylamine*, which separated from chloroform in yellow prisms (Found: C, 49·4; H, 3·4%) and changed to a red polymorphic form, m. p. 183°, on heating.

3-*Methyl*-4 : 6 : 2′ : 4′-*tetranitrodiphenylamine*.—(*a*) 3-Methyl-2′ : 4′-dinitrodiphenylamine (5 g.) was heated on the steam-bath with concentrated sulphuric acid (10 c.c.) and nitric acid (20 c.c.; *d* 1·42) until the solution became pale yellow (about ½ hour). When cold, the mixture was poured on ice, and the precipitated **3-*methyl*-4 : 6 : 2′ : 4′-*tetranitrodiphenylamine*** separated from acetic acid in yellow plates (2·5 g.), m. p. 208—209° (Found : C, 43·7; H, 2·6%). (*b*) 3-Methyl-4 : 6-dinitrodiphenylamine (0·5 g.; Borsche and Fiedler, *Ber.*, 1913, **46**, 2117) was kept for a few minutes with nitric acid (5 c.c.; *d* 1·42), the whole heated for 20 minutes on the steam-bath, then poured on ice, and the solid crystallised from acetic acid; the same tetranitro-compound (0·5 g.) was obtained.

3-*Methyl*-4 : 6 : 4′-*trinitrodiphenylamine*.—After 3-methyl-4 : 6-dinitrodiphenylamine (0·5 g.) had been left with nitric acid (5 c.c.; *d* 1·42) at room temperature for 5 minutes and the whole poured on ice, **3-*methyl*-4 : 6 : 4′-*trinitrodiphenylamine***, yellow needles (0·5 g.), m. p. 207° (from acetic acid), was precipitated (Found : C, 49·4; H, 2·9%). The same compound (2 g.) was obtained when a mixture of 1-chloro-3-methyl-4 : 6-dinitrobenzene (2·2 g.), *p*-nitroaniline (1·5 g.), and diethylaniline (5 c.c.) was heated at 190° for 2 hours and then extracted with hot glacial acetic acid (15 c.c.), the solution poured into dilute hydrochloric acid, and the product crystallised from acetic acid.

6-*Cyano*-3-*methylcarbazole*.—A hot solution of stannous chloride (45 g.) in concentrated hydrochloric acid (100 c.c.) was added to 4′-cyano-4-methyl-2′-nitrodiphenylamine (9 g.; Mattaar, *Rec. Trav. chim.*, 1922, **41**, 24) in boiling glacial acetic acid, and the whole boiled until the colour became deep yellow (about 5 minutes). When cold, the mixture was made alkaline with aqueous sodium hydroxide, and the solid filtered off and crystallised from ethanol (200 c.c.), from which **2′-*amino*-4′-*cyano*-4-*methyldiphenylamine*** separated in colourless plates (6 g.), m. p. 162—163° (Found : C, 75·0; H, 6·0. $C_{14}H_{13}N_3$ requires C, 75·3; H, 5·8%). The derived **5-*cyano*-1-*p*-*tolylbenzotriazole*** crystallised from ethanol in colourless needles, m. p. 199° (Found : C, 71·7; H, 4·4. $C_{14}H_{10}N_4$ requires C, 71·8; H, 4·3%). This substance (3 g.) was heated gradually from 320° to 380°, the residue was twice extracted with hot ethanol (60 c.c.), the united extracts were boiled with charcoal, and the product was precipitated from the filtered solution by dilution with water (in the preparation of all the substituted carbazoles described below the reaction product was similarly treated before crystallisation). **6-*Cyano*-3-*methylcarbazole*** crystallised from ethanol in colourless plates (1·5 g.), m. p. 183—184° (Found : C, 81·5; H, 4·8. $C_{14}H_{10}N_2$ requires C, 81·6; H, 4·9%).

4′-*Cyano*-4-*methyl*-2 : 6 : 2′-*trinitrodiphenylamine*.—(*a*) When 4′-cyano-4-methyl-2′-nitrodiphenylamine (10 g.) was heated for several hours on the steam-bath with nitric acid (100 c.c.; *d* 1·3) and the solid obtained by dilution with water was crystallised from ethanol, **4′-*cyano*-4-*methyl*-2 : 6 : 2′-*trinitrodiphenylamine*** was obtained in yellow needles (6 g.), m. p. 188° (Found : C, 48·9; H, 2·5. $C_{14}H_9O_6N_5$ requires C, 49·0; H, 2·6%). (*b*) After a mixture of 4-methyl-2 : 6-dinitrophenyl toluene-*p*-sulphonate (2 g.) and *p*-aminobenzonitrile (2 g.) had been heated at 180° for 20 minutes and then crystallised from ethanol, **4′-*cyano*-4-*methyl*-2 : 6-*dinitrodiphenylamine*** was isolated in red prisms (0·5 g.), m. p. 156—158° (Found : C, 56·2; H, 3·4. $C_{14}H_{10}O_4N_4$ requires C, 56·4; H, 3·4%). When this substance (0·3 g.) was heated with nitric acid (3 c.c.; *d* 1·42) at 90° for 2 minutes, the whole poured into water, and the product crystallised from ethanol, the trinitro-compound (0·25 g.), identical (mixed m. p.) with the above material, was obtained.

2-*Cyano*-7-*methylphenazine*.—After a mixture of 3-nitro-*p*-toluidine (5 g.), 4-chloro-3-nitrobenzonitrile (5·5 g.), and potassium carbonate (4 g.) had been heated at 170° for ½ hour and then ground with dilute hydrochloric acid, and the product crystallised from ethanol (charcoal), **4′-*cyano*-4-*methyl*-2 : 2′-*dinitrodiphenylamine*** was obtained in orange needles (3 g.), m. p. 244° (Found : C, 56·0; H, 3·4%). When reduced with sodium sulphide as described for 2-methyl-4 : 2′ : 4′-trinitrodiphenylamine, this substance gave **2-*cyano*-7-*methylphenazine***, which separated from ethanol in pale yellow plates, m. p. 248° (Found : C, 76·4; H, 4·1. $C_{14}H_9N_3$ requires C, 76·7; H, 4·1%).

6-*Cyano*-1-*methylcarbazole*.—Prepared from 4′-cyano-2-methyl-2′-nitrodiphenylamine (m. p. 121°; compare Mattaar, *loc. cit.*) like the isomerides described above, **2′-*amino*-4′-*cyano*-2-*methyldiphenylamine*** separated from ethanol in colourless needles, m. p. 154° (Found : C, 75·0; H, 6·0%), and **5-*cyano*-1-*o*-*tolylbenzotriazole*** from aqueous ethanol in colourless plates, m. p. 100° (Found : C, 71·7; H, 4·4%). The latter (2 g.) was heated from 290° to 340° during ½ hour, and the **6-*cyano*-1-*methylcarbazole*** obtained from aqueous ethanol in pale yellow needles (1·25 g.), m. p. 230° (Found : C, 81·4; H, 5·1%).

6-*Cyano*-1-*methyl*-3-*nitrocarbazole*.—When nitric acid (25 c.c.; *d* 1·42) was added below 20° to 4′-cyano-2-methyl-2′-nitrodiphenylamine (8 g.) in glacial acetic acid (150 c.c.), **4′-*cyano*-2-*methyl*-4 : 2′-*dinitrodiphenylamine*** (7·5 g.), m. p. 231—232°, gradually separated in red plates. The same compound (4 g.) was obtained when the product of heating a mixture of 5-nitro-*o*-toluidine (7 g.), 4-chloro-3-nitrobenzonitrile (7·5 g.), and potassium carbonate (6 g.) at 150—160° was ground with dilute hydrochloric acid and crystallised from acetic acid (Found : C, 56·3; H, 3·5%). It was converted into **2′-*amino*-4′-*cyano*-2-*methyl*-4-*nitrodiphenylamine***, orange-yellow needles, m. p. 210—211° (from ethanol) (Found : C, 62·7; H, 4·4. $C_{14}H_{12}O_2N_4$ requires C, 62·7; H, 4·5%), and **5-*cyano*-1-(2-*methyl*-4-*nitrophenyl*)*benzotriazole***, orange prisms, m. p. 220—221° (from ethanol) (Found : C, 60·2; H, 3·1. $C_{14}H_8O_2N_4$ requires C, 60·2; H, 3·2%). The latter (2 g.) was heated gradually from 280° to 310°; when the product, isolated as before, was crystallised from benzene–light petroleum (b. p. 60—80°), **6-*cyano*-1-*methyl*-3-*nitrocarbazole*** was obtained in pale yellow needles (0·15 g.), m. p. 348—350° (Found : C, 66·4; H, 3·6. $C_{14}H_9O_2N_3$ requires C, 66·9; H, 3·6%).

4′-*Cyano*-2-*methyl*-4 : 6 : 2′-*trinitrodiphenylamine*.—This *compound* was obtained when a mixture of the above dinitro-compound (2 g.; m. p. 231—232°), glacial acetic acid (50 c.c.), and nitric acid (15 c.c.; *d* 1·42) was heated on the steam-bath until a clear yellow solution resulted, and then poured into water; it crystallised from acetic acid in pale yellow prisms (2 g.), m. p. 221° (Found : C, 48·7; H, 2·6%).

3-*Chloro*-6-*nitrocarbazole*.—Two portions of 1-*p*-chlorophenyl-5-nitrobenzotriazole (each 1·5 g., prepared as described by Blom, *loc. cit.*) were heated separately at 350° (metal-bath) for 10 minutes in a flask with a long neck, the sublimate of unchanged triazole being decomposed with a free flame. 3-Chloro-6-nitrocarbazole was obtained from benzene in pale yellow needles (0·2 g.), m. p. 284° (Found: C, 58·8; H, 2·8. Calc. for $C_{12}H_7O_2N_2Cl$: C, 58·4; H, 2·8%). The use of larger quantities of material, or higher temperatures, led to explosions. This substance has been prepared in other ways (Lamberti-Zanardi, *Gazzetta*, 1896, **26**, 289; D.R.-P. 295,817, *Chem. Zentr.*, 1917, i, 295).

4-*Chloro*-2 : 2′ : 4′-*trinitrodiphenylamine*.—(*a*) When 4-chloro-2′ : 4′-dinitrodiphenylamine (8 g.) was treated with nitric acid (70 c.c.; *d* 1·23) for ½ hour at 90°, the red colour of the suspended solid became yellow. After dilution with water, the product was crystallised from acetic acid, and 4-*chloro*-2 : 2′ : 4′-*trinitrodiphenylamine* obtained in orange-yellow needles (7·5 g.), m. p. 186° (Found: C, 42·7; H, 2·1. $C_{12}H_7O_6N_4Cl$ requires C, 42·5; H, 2·1%). (*b*) When a mixture of 4-chloro-2-nitroaniline (1·7 g.), 1-chloro-2 : 4-dinitrobenzene (2 g.), and potassium carbonate (2 g.) was heated at 180° for an hour and the product was washed with hot dilute hydrochloric acid and crystallised from acetic acid, the same trinitro-compound (mixed m. p.) was isolated in golden-yellow needles (1·5 g.), m. p. 185°.

4-*Chloro*-2 : 6 : 2′ : 4′-*tetranitrodiphenylamine*.—The above trinitro-compound (1 g.) dissolved when heated on the steam-bath with nitric acid (30 c.c.; *d* 1·42), and, after dilution with water, the precipitated 4-*chloro*-2 : 6 : 2′ : 4′-*tetranitrodiphenylamine* crystallised from acetic acid in lemon-yellow needles (1 g.), m. p. 215° (Found: C, 37·4; H, 1·8. $C_{12}H_4O_8N_5Cl$ requires C, 37·5; H, 1·6%). The same compound (m. p. and mixed m. p. 215°) was isolated when 4-chloro-2 : 6-dinitrodiphenylamine (Ullmann and Sané, *loc. cit.*) was nitrated under similar conditions.

4-*Chloro*-3 : 2′ : 4′-*trinitrodiphenylamine*.—After 4-chloro-3-nitroaniline (1·7 g.), 1-chloro-2 : 4-dinitrobenzene (2 g.), and anhydrous sodium acetate (1 g.) had been heated together at 180° for an hour and the product extracted with hot acetic acid, 4-*chloro*-3 : 2′ : 4′-*trinitrodiphenylamine*, yellow needles (1·5 g.), m. p. 179—180° (from ethanol), separated on cooling (Found: C, 42·7; H, 2·3%). The derived 2′-*amino*-4-*chloro*-3 : 4′-*dinitrodiphenylamine* was extracted from the crude reduction product (dried at 100°) with boiling benzene (charcoal) and recovered by the addition of light petroleum (b. p. 60—80°); it separated from benzene–light petroleum in dark red needles, m. p. 194° (Found: C, 46·7; H, 3·0. $C_{12}H_9O_4N_4Cl$ requires C, 46·7; H, 2·9%). After the trinitro-compound (1 g.) had been refluxed with aniline (10 c.c.) for 3 hours and the mixture treated with dilute hydrochloric acid, the solid was washed with a little ethanol and twice recrystallised from acetic acid; 4-*anilino*-3 : 2′ : 4′-*trinitrodiphenylamine* was obtained in red plates (0·5 g.), m. p. 197—198° (Found: C, 54·0; H, 3·3. $C_{18}H_{13}O_6N_5$ requires C, 54·7; H, 3·3%).

1-*Chloro*-6-*nitrocarbazole*.—Prepared from 2-chloro-2′ : 4′-dinitrodiphenylamine, 2′-amino-2-chloro-4′-nitrodiphenylamine crystallised from ethanol in red prisms, m. p. 112° [compare Fries (*Annalen*, 1927, **454**, 206), who gives m. p. 117°; a polymorphic form (orange needles) melted at 90° and resolidified to the red form], and 1-o-*chlorophenyl*-5-*nitrobenzotriazole* from ethanol in colourless needles, m. p. 130° (Found: C, 52·6; H, 2·6. $C_{12}H_7O_2N_4Cl$ requires C, 52·5; H, 2·6%). When the latter (4 g.) was heated in two portions, evolution of nitrogen began at 310—320° and was complete after a short time at 360°. 1-*Chloro*-6-*nitrocarbazole* crystallised from benzene (charcoal) in golden yellow prisms (0·5 g.), m. p. 254° (Found: C, 58·4; H, 3·0%).

1-(2-*Chloro*-4-*nitrophenyl*)-5-*nitrobenzotriazole*.—Prepared from 2-chloro-4 : 2′ : 4′-trinitrodiphenylamine (7 g.; Reverdin and Crépieux, *loc. cit.*), the crude 2′-*amino*-2-*chloro*-4 : 4′-*dinitrodiphenylamine* was dried and extracted with boiling benzene, and the extract boiled with charcoal, filtered, and treated while still boiling with light petroleum until crystallisation began. The amine was recrystallised from benzene–light petroleum and obtained in brown prisms (4 g.), which changed at 180° to a yellow form, m. p. 210° (Found: C, 46·8; H, 2·8%). 1-(2-*Chloro*-4-*nitrophenyl*)-5-*nitrobenzotriazole* crystallised from ethanol in colourless plates, m. p. 149° (Found: C, 45·0; H, 1·8. $C_{12}H_6O_4N_5Cl$ requires C, 45·1; H, 1·9%).

2-*Chloro*-4 : 6 : 2′ : 4′-*tetranitrodiphenylamine*.—(*a*) After 2-chloro-4 : 2′ : 4′-trinitrodiphenylamine (2 g.) had been heated on a steam-bath for an hour with nitric acid (50 c.c.; *d* 1·42), addition of water precipitated 2-*chloro*-4 : 6 : 2′ : 4′-*tetranitrodiphenylamine*, yellow needles (2 g.), m. p. 191° (from acetic acid) (Found: C, 38·0; H, 1·6%). (*b*) Anhydrous sodium carbonate (12 g.) was gradually added to a mixture of 2-chloro-4 : 6-dinitrophenol (22 g.), toluene-*p*-sulphonyl chloride (20 g.), and water (40 c.c.) heated on a steam-bath, and after ½ hour the whole was extracted several times with warm dilute sodium carbonate solution (cf. Ullmann and Sané, *loc. cit.*). The residue was twice recrystallised from benzene, and 2-*chloro*-4 : 6-*dinitrophenyl toluene*-p-*sulphonate* obtained in colourless needles (25 g.), m. p. 155° (Found: C, 42·4; H, 2·7. $C_{13}H_9O_7N_2ClS$ requires C, 41·9; H, 2·4%). After this compound, (3 g.) had been heated with aniline (15 c.c.) at 90° for 2 hours, an equal volume of ethanol was added, and the whole poured into an excess of dilute hydrochloric acid. The precipitated 2-chloro-4 : 6-dinitrodiphenylamine separated from ethanol in orange plates (1·5 g.), m. p. 140° (Found: C, 49·4; H, 3·0. Calc. for $C_{12}H_8O_4N_3Cl$: C, 49·1; H, 2·7%). Ullmann and Sané (*loc. cit.*) made this substance from aniline and 1 : 2-dichloro-4 : 6-dinitrobenzene, but gave no m. p. The compound (1 g.) rapidly dissolved in nitric acid (30 c.c.; *d* 1·42) at 90°, and water then precipitated the above tetranitro-derivative (1 g.).

1-*Chloro*-3-*nitrocarbazole*.—Prepared from 2-chloro-4 : 6-dinitrodiphenylamine, 6-amino-2-chloro-4-nitrodiphenylamine separated from aqueous ethanol in brown plates, m. p. 122—124°, and was converted without further purification into 7-*chloro*-5-*nitro*-1-*phenylbenzotriazole* pale brown prisms, m. p. 209° (from ethanol) (Found: C, 53·0; H, 2·7%). This compound (1 g.) was heated at 320° until effervescence ceased, and, after crystallisation twice from toluene and then from aqueous ethanol, 1-*chloro*-3-*nitrocarbazole* was obtained in pale yellow needles (0·25 g.), m. p. 206° (Found: C, 58·8; H, 2·5%).

3-*Chloro*-6-*cyanocarbazole*.—After a mixture of *p*-chloroaniline (10 g.), 4-chloro-3-nitrobenzonitrile (10 g.), and anhydrous sodium acetate (7 g.) had been heated at 165° for ½ hour and the product extracted

with boiling ethanol, 4-*chloro*-4′-*cyano*-2′-*nitrodiphenylamine* crystallised from the solution, on cooling, in orange-red needles (14 g.), m. p. 165° (Found : C, 57·2; H, 3·4. $C_{13}H_8O_2N_3Cl$ requires C, 57·0; H, 2·9%). A hot solution of stannous chloride (10 g.) in concentrated hydrochloric acid (20 c.c.) was added to a boiling solution of this compound (2 g.) in glacial acetic acid, and after a few minutes the mixture was cooled and made strongly alkaline with concentrated aqueous sodium hydroxide. The solid was extracted with boiling ethanol, and the product which separated from the extract on cooling yielded 2′-*amino*-4-*chloro*-4′-*cyanodiphenylamine*, almost colourless needles (1·5 g.), m. p. 209° (from ethanol) (Found : C, 64·7; H, 4·3. $C_{13}H_{10}N_3Cl$ requires C, 64·1; H, 4·1%). The derived 1-p-*chlorophenyl*-5-*cyanobenzotriazole* crystallised from acetic acid in colourless needles, m. p. 298° (Found : C, 61·5; H, 2·9. $C_{19}H_7N_4Cl$ requires C, 61·3; H, 2·8%). The triazole (1 g.) was heated at 380° for 20 minutes. When the material extracted as before was crystallised from a little ethanol, unchanged triazole separated, and, after this had been removed, 3-*chloro*-6-*cyanocarbazole* was obtained by the addition of water. The latter process was repeated and the substance was finally isolated from aqueous ethanol in colourless needles (0·2 g.) m. p. 250° (Found : C, 68·5; H, 3·4. $C_{13}H_7N_2Cl$ requires C, 68·9; H, 3·1%).

7-*Chloro*-2-*cyanophenazine*.—After 4-chloro-4′-cyano-2′-nitrodiphenylamine (10 g.) had been heated on a steam-bath with nitric acid (100 c.c.; *d* 1·23) for an hour, water precipitated 4-*chloro*-4′-*cyano*-2 : 2′-*dinitrodiphenylamine*, orange-red needles (10 g.), m. p. 241° (from acetic acid) (Found : C, 49·3; H, 2·1. $C_{13}H_7O_4N_4Cl$ requires C, 49·0; H, 2·2%). When reduced with sodium sulphide as described for 2-methyl-4 : 2′ : 4′-trinitrodiphenylamine, it gave 7-*chloro*-2-*cyanophenazine*, pale yellow needles, m. p. 317° (from amyl alcohol) (Found : C, 65·2; H, 2·6. $C_{13}H_6N_3Cl$ requires C, 65·1; H, 2·5%).

5-(5-*Cyanobenzotriazol*-1-*yl*)-1-*phenylbenzotriazole*.—A mixture of 4-chloro-3-nitroaniline (8 g.), 4-chloro-3-nitrobenzonitrile (8 g.), and potassium carbonate (6 g.) was heated at 160° with stirring for 20 minutes and then extracted with warm dilute hydrochloric acid, and the residue crystallised from acetic acid (charcoal); 4-*chloro*-4′-*cyano*-3 : 2′-*dinitrodiphenylamine* separated in orange needles (4 g.), m. p. 224° (Found : C, 49·2; H, 2·5%). After this substance (4 g.) had been treated with aniline as described for 4-anilino-3 : 2′ : 4′-trinitrodiphenylamine, 4-*anilino*-4′-*cyano*-3 : 2′-*dinitrodiphenylamine*, red plates (2 g.), m. p. 215° (from acetic acid), was obtained (Found : C, 60·2; H, 4·0. $C_{19}H_{13}O_4N_5$ requires C, 60·8; H, 3·5%). Stannous chloride (10 g.) in concentrated hydrochloric acid (30 c.c.) was added to a hot solution of the anilino-compound (2 g.) in glacial acetic acid (100 c.c.), and the mixture was boiled for 5 minutes, cooled, and immediately treated with aqueous sodium nitrite (1·5 g.). Addition of dilute hydrochloric acid precipitated 5-(5-*cyanobenzotriazol*-1-*yl*)-1-*phenylbenzotriazole*, almost colourless prisms (1 g.), m. p. 310—312° [from acetic acid (charcoal)] (Found : C, 67·2; H, 3·3. $C_{19}H_{11}N_7$ requires C, 67·7; H, 3·3%).

1-*Chloro*-6-*cyanocarbazole*.—After a mixture of *o*-chloroaniline (15 c.c.), 4-chloro-3-nitrobenzonitrile (10 g.), and anhydrous sodium acetate (7 g.) had been heated at 205° for 2 hours, ethanol (50 c.c.) added, and the whole poured into dilute hydrochloric acid, 2-*chloro*-4′-*cyano*-2′-*nitrodiphenylamine*, orange-yellow needles (6 g.), m. p. 164—165° (from ethanol), was precipitated (Found : C, 57·4; H, 2·8%). Prepared like the isomeride described above, 2′-*amino*-2-*chloro*-4′-*cyanodiphenylamine* separated from ethanol in colourless needles, m. p. 151° (Found : C, 64·2; H, 4·3%), and the derived 1-*o*-*chlorophenyl*-5-*cyanobenzotriazole* crystallised from ethanol in colourless prisms, m. p. 138° (Found : C, 61·4; H, 2·9%). The triazole (1·5 g.) was heated at 350° until evolution of nitrogen ceased, and 1-*chloro*-6-*cyanocarbazole*, pale brown prisms (0·2 g.), m. p. 247° (from aqueous ethanol), was obtained (Found : C, 69·3; H, 3·2%).

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26. *Fluorescence Quenching by Colloid Anions and Cations.*

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The fluorescence of solutions of certain basic and acidic dyes is quenched by the addition of small quantities of colloid anions and cations respectively. The magnitude of the effect, and its reversal by electrolytes are described. Possible explanations and applications of the effect are discussed.

AQUEOUS solutions of fluorescent dyes lose their fluorescence on concentration (Perrin, *J. Chim. physique*, 1928, **25**, 531) or on the addition of electrolytes, (Kortüm, *Z. physikal. Chem.*, 1938, *B*, **40**, 431). With particular groups of dyes, for example, the polymethine dyes (Scheibe, *Kolloid-Z.*, 1938, **82**, 1), the quenching of fluorescence has been shown to follow the aggregation of the dye molecules in solution. Bowen (*Quart. Reviews*, 1947, **1**, 1), in a review of work on fluorescence quenching, expresses the view that generally the monomeric dye is fluorescent whereas aggregates of two or more molecules are non-fluorescent.

Rabinowitch and Epstein (*J. Amer. Chem. Soc.*, 1941, **63**, 69) drew attention to the similarity between dyes and soaps; both contain large hydrocarbon portions to which strongly polar groups are attached, and many dyes show, in concentrated solution, the changes in viscosity and conductivity characteristic of the formation of colloidal aggregates in soap solutions.

A phenomenon similar to the quenching of fluorescence of dye solutions on concentration or the addition of salts is the metachromatic effect. Certain basic dyes, for example, toluidine-blue

and thionine, change in colour when treated in aqueous solution with a colloidal anion, for example, heparin or agar-agar. Michaelis and Granick (*ibid.*, 1945, **67**, 1212) have shown that this colour change also occurs when solutions of metachromatic dyes are concentrated or treated with electrolytes. They attributed the effect to the aggregation of the dye molecules by the colloidal anion, and demonstrated that the absorption spectrum of the monomeric dye differed from that of the aggregated dye. Similar to the metachromatic effect is the quenching of fluorescence of dye solutions by colloidal ions. The most familiar example of this phenomenon is the use of fluorescein-type dyes to indicate the charge on silver halide sols in the volumetric analysis of halides with silver nitrate (Fajans and Wolff, *Z. anorg. Chem.*, 1924, **137**, 221). There appears, however, to be no record of quantitative measurements of the quenching of fluorescence by colloid anions and cations.

During investigations of the properties of water-soluble, strongly acidic or basic colloids a convenient method for their analysis was required. The metachromatic colour change of basic dyes provided a basis for the analysis of colloid anions; the dyes were not, however, affected by colloid cations. Colour changes were noted on similar treatment of many acidic dyes, but no dye was particularly suitable for colorimetric estimation. It was noted, however, that the fluorescence of fluorescein and similar dyes was completely quenched by small concentrations of colloid cations. Similarly the fluorescence of rhodamine and other basic dyes was quenched by colloid anions.

It was found convenient to use the fluorescence-quenching properties for analysis of the colloid ions and for examination of their behaviour in solutions. A detailed description of these uses will be given later.

The quenching of fluorescence by colloid ions resembled closely the metachromatic effect, and like it appeared to be caused by aggregation of fluorescent monomeric dye ions by the colloid ion to form non-fluorescent aggregates. Unlike the metachromatic effect, however, the quenching of fluorescence was extremely sensitive to the presence of electrolytes. For example, the fluorescence of dichlorofluorescein quenched by a colloid cation could be restored by a concentration of a tervalent anion as low as 10^{-6} M.

The phenomenon of fluorescence quenching by colloid ions showed, therefore, features of general interest quite apart from its particular uses in the analytical methods mentioned above. A limited experimental examination of the quenching of fluorescence of dichlorofluorescein and Rhodamine 6G by colloid cations and anions respectively was therefore made. This paper describes these experiments and discusses some possible explanations of the phenomenon.

Experimental.

Measurement of Fluorescence.—Flourescence and its quenching were measured in a simple fluorimeter which consisted of a 100-w. projection lamp, the light from which was passed *via* a lens through a boiling-tube containing the dye solution. Light scattered by fluorescence was measured by means of a barrier-layer-type photoelectric cell connected to a galvanometer. This instrument was calibrated against known concentrations of the dyes.

Materials.—The dyes used were dichlorofluorescein as the free acid, and Rhodamine 6G as chloride, of the grade normally used in adsorption titrations. Dichlorofluorescein was dissolved in 0·1% aqueous pyridine to avoid changes in fluorescence caused by contamination of the solution with traces of acid on the surfaces of the glassware. This precaution was not necessary with Rhodamine 6G, which was dissolved in distilled water.

Colloid Ions.—The colloid anion used in these experiments was sodium polyvinyl sulphate, prepared by treating polyvinyl alcohol with chlorosulphonic acid–pyridine (Lintot, *Arch. Biol.*, 1934, **46**, 509). The product was purified by repeated dissolution in water and precipitation with ethanol. The final material was a hygroscopic white powder, in which approx. 50% of the hydroxyl groups of the polyvinyl alcohol were esterified.

The colloid cation used was poly-(1-methyl-2-vinylpyridinium iodide). This was prepared by exposing redistilled 2-vinylpyridine to ultra-violet light in a quartz cell at room temperature for several days. The polymer produced was separated from unchanged monomer by gently warming the mixture *in vacuo* and was used in the next stage without further purification; the polyvinylpyridine was dissolved in 2 moles of methyl iodide at room temperature and the methiodide slowly precipitated during about 24 hours; unchanged methyl iodide was decanted and the quaternary salt purified by repeated dissolution in water and precipitation with acetone; during the later stages of the purification, the polymer tended to form a sol in the acetone and it was necessary to add a small quantity of potassium nitrate to assist precipitation; the final product was a hydroscopic yellow powder; titration with silver nitrate indicated that 70% of the polyvinylpyridine units of the molecule had been converted into quaternary salts.

Results.

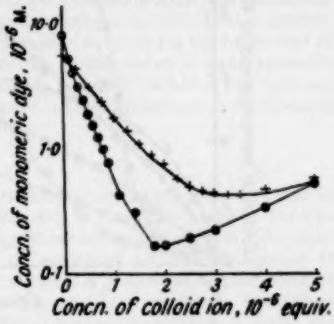
In view of the rather uncertain composition of the colloid ions the strengths of their solutions are expressed in terms of equivalence rather than as mass per unit volume. One equivalent of

sodium polyvinyl sulphate or of poly-(1-methyl-2-vinylpyridinium iodide) is defined as that quantity possessing $6{\cdot}02 \times 10^{23}$ ionogenic groupings.

Fig. 1 shows the quenching fluorescence of dichlorofluorescein by poly-(1-methyl-2-vinylpyridinium iodide), and of Rhodamine 6G by sodium polyvinyl sulphate; the concentration of the dyes is plotted logarithmically and is calculated on the assumption that the fluorescence remaining in the solution after successive additions of colloid anion or cation is due to free non-associated dye. It is realised that compounds formed by the colloid ion with the dye or with the associated dye may well have some fluorescence, but the assumption that they have none was thought justified since in both cases the fluorescence of the mixture was reduced almost to zero when sufficient colloid ion had been added. The diagrams show that the reaction occurs in two stages. Up to the addition of 2—3 equivalents of colloid ion fluorescence is quenched until less than 5% of the free dye remains in solution. Further additions cause a slow restoration of fluorescence.

FIG. 1.

The quenching of fluorescence of Rhodamine 6G (× × ×) and dichlorofluorescein (○ ○ ○) by sodium polyvinyl sulphate and poly-(1-methyl-2-vinylpyridinium iodide) respectively.

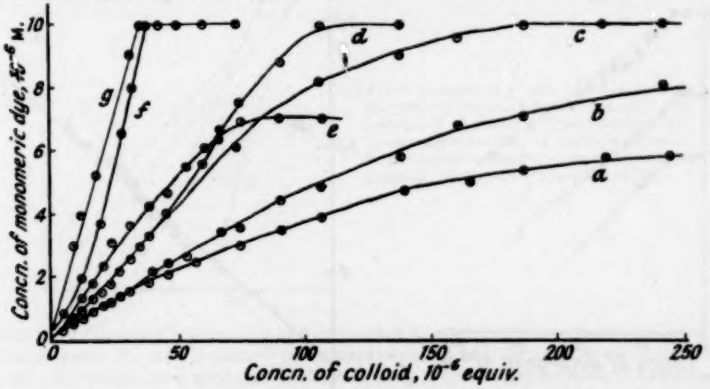


It will be shown later that the addition of salts to the dye–colloid ion complex restores the fluorescence of the solution. It is likely, therefore, that the restoration of fluorescence following the addition of an excess of colloid ion is caused by a similar salt effect.

Effects of Salts on the Dye–Polyion Complex.—Fig. 2 shows the effect of adding various salts to a mixture of dichlorofluorescein and poly-(1-methyl-2-vinylpyridinium iodide). The salts used in this series of experiments all possessed univalent anions. All produced a restoration of the fluorescence, presumably by dissociating the dye–colloid ion complex. But three main groups of salts all restoring fluorescence in a different manner are discernible. First, low-

FIG. 2.

The restoration of fluorescence by the addition of univalent anions to a mixture of dichlorofluorescein and poly-(1-methyl-2-vinylpyridinium iodide). a, *Sodium acetate*; b, *sodium chloride*, c, *potassium chloride*; d, *lithium chloride*; e, *sodium iodide*; f, *sodium oleate*; g, *sodium cetyl sulphate.*



molecular-weight salts of strong acids and strong bases, *e.g.*, sodium chloride, potassium bromide, lithium chloride, with which the restoration of fluorescein anion from the complex proceeds until all, or nearly all, the dye has been liberated. Secondly, salts of strong bases with weak acids of low molecular weight, with which the liberation of dye from the complex is incomplete. Thirdly, salts of strong bases and high-molecular-weight acids, with which there is a stoicheio-

metric combination between the salt anion and the colloid cation leading to the liberation of all the dye when one molecular equivalent of salt has been added.

FIG. 3.

The restoration of fluorescence by the addition of bi-, ter-, and quadri-valent ions to a mixture of dichlorofluorescein and poly-(1-methyl-2-vinylpyridinium iodide). a, *Magnesium sulphate,* 10^{-4} M.; b, *potassium oxalate,* 10^{-4} M.; c, *sodium sulphate,* 10^{-4} M.; d, *potassium ferricyanide,* 10^{-4} M.; e, *potassium ferrocyanide,* 10^{-4} M.; f, *sodium citrate,* 10^{-4} M.

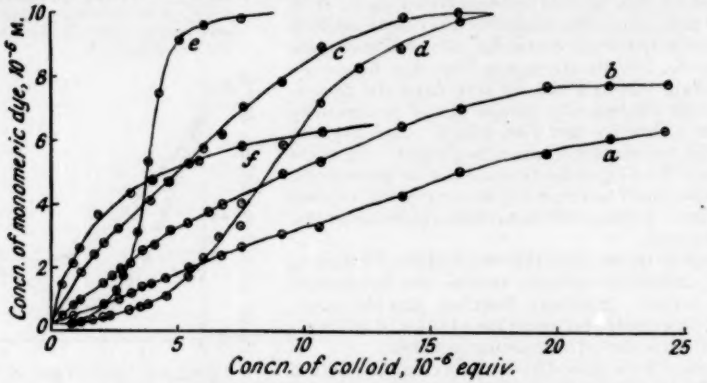


Fig. 3 shows a comparison of the effects of adding uni-, bi-, ter-, and quadri-valent anions to the dye–colloid ion complex. The salts used in this series were all of strong bases and strong acids of relatively low molecular weight. The restoration of free dichlorofluorescein from the

FIG. 4.

The use of dichlorofluorescein as an indicator of the state of aggregation of benzylhexadecyldimethylammonium chloride.

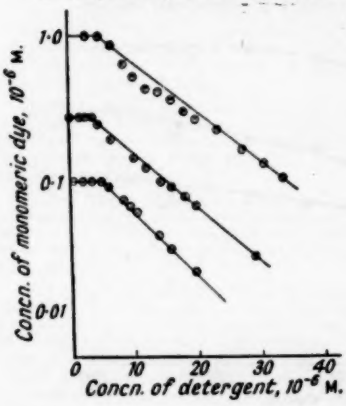
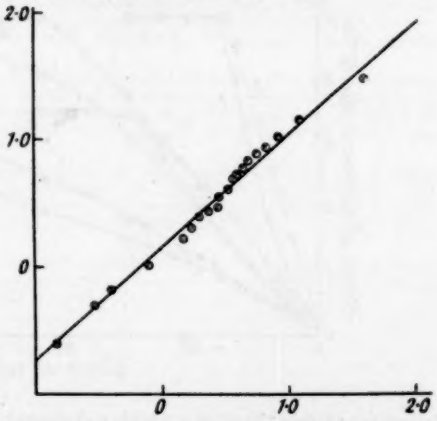


FIG. 5.

The relation between the proportion of fluorescence quenched by unit quantity of poly-(1-methyl-2-vinylpyridinium iodide) and the concentration of dye remaining in solution in a fluorescent state (ordinate). The data for this relation are derived from Fig. 1 *and are plotted in logarithmic units.*



complex occurs with increasing ease as the valency of the anion is raised. The ratios of the concentration of anions of various valency necessary to restore fluorescence to the same extent falls much in the same order as the concentrations of the same salts necessary to precipitate negatively charged colloids. The restoration of the fluorescence of Rhodamine, from its complex with

polyvinyl sulphate, by cations was closely similar. The relationship between cation concentration and the extent of fluorescence restoration depended on the valency and size of the cation used.

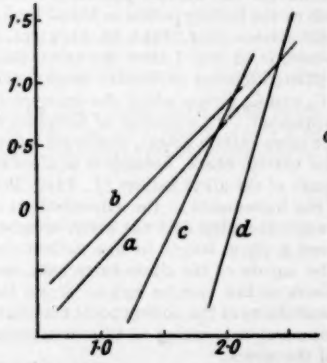
Suppression of Fluorescence by Detergents.—Fig. 4 shows the suppression of the fluorescence of dichlorofluorescein by benzylhexadecyldimethylammonium chloride : after a certain limiting quantity of the cationic detergent has been added, an effect occurs closely similar to that given by the colloid cation. It is well known that detergents above a certain limiting concentration exist in solution as colloidal aggregates. Such aggregates are obviously similar in structure to the colloid ions. The concentration of detergent at which fluorescence quenching commences is the same as that at which an abrupt change in conductivity occurs (Hartley and Runnicles, *Proc. Roy. Soc., A*, **1938**, **168**, 420). This observation, and the indication from Fig. 2 that the limiting concentration of detergent at which quenching occurs is independent of the dye concentration, suggest that measurements of this type might prove useful in studying the behaviour of detergent solutions. Michaelis (*J. Phys. Coll. Chem.*, **1950**, **54**, 1) has shown a metachromatic effect to occur with anionic soaps and basic dyes and similarly suggests the use of the latter as indicators of the colloidal state of anionic detergent solutions. The fluorescence of Rhodamine 6G is, as might be expected, quenched by anionic detergents.

Discussion.

The changes in absorption spectra of the metachromatic basic dyes on reaction with colloid anions have been attributed by Michaelis and Granick (*loc. cit.*) to the aggregation of the dye molecules by the colloid ions. The fluorescence-quenching phenomena described in this paper resemble the metachromatic effect and could similarly be explained by the aggregation of fluorescent dye molecules by the colloid ions. The ready reversal of fluorescence quenching by ions of the same sign as the dye ion suggests, however, that adsorption of the dye by the colloid ion, rather than aggregation, is responsible for the fluorescence quenching. Fig. 5 shows the quenching of fluorescence of dichlorofluorescein by poly-(1-methyl-2-vinylpyridinium iodide) plotted to illustrate the relation between the proportion of dye " adsorbed " by a unit quantity of colloid cation and the dye concentration remaining in solution. The linear relation over a wide range of values is in accord with the Freundlich adsorption isotherm.

Fig. 6.

The adsorption of anions by poly-(1-methyl-2-vinylpyridinium iodide).



Ordinate : proportion of salt adsorbed by unit quantity of poly-cation. Abscissa : concentration of anion. Both quantities are in logarithmic units. a, *Sodium chloride*; b, *potassium bromide*; c, *potassium ferricyanide*; d, *potassium ferrocyanide.*

Regardless of the exact mechanism of fluorescence quenching, it is probable that the restoration of fluorescence by salts is caused by adsorption of the added ions by the colloid, leading either to its inactivation as a quencher of fluorescence, or to the displacement of adsorbed dye. Fig. 6 shows the relation between the proportion of various ions adsorbed by poly-(1-methyl-2-vinylpyridinium iodide) and the concentration of the ions. The proportion of the ions adsorbed by the colloid was calculated on the assumption that the quantity of ion adsorbed was equivalent to the quantity of dye restored to a fluorescent condition. The linear nature of the relation appears to confirm this assumption.

This interaction between the colloid ions and the fluorescent dyes appears, therefore, to be

sufficiently slight to enable the latter to be used as internal indicators of the charge on colloid ions. Michaelis's suggestion that metachromatic dyes would be of value as internal indicators of the colloidal state of detergents is thus confirmed and extended to other colloid types.

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27. *Atom Polarisation. Part II. Relationships between Molecular Dimensions and Boiling Points for Branched-chain Paraffins.*

By Arnold Audsley and Frank R. Goss.

Exaltations of molecular volume and of refraction for branched-chain paraffins are negative and directly related to the extent of the chain-branching when the exaltations are measured at the boiling point, or more strictly in the gaseous state. As, however, the boiling points themselves are not related to the molecular shape in the same simple manner, the molecular functions have, at 20°, values which, although their sequence is changed, fall on a series of characteristic curves.

Atom polarisation and dispersion are not noticeably affected by chain-branching, and consequently the exaltations of refraction and polarisation are identical within narrow limits and the polarisations fall on the same series of curves as the refractions.

Sensitive methods for the detection of impurities, particularly those of high dielectric constant, can be based on these properties of the hydrocarbons.

Relationships between Molecular Volume and Boiling Point.—In a comparison of the molecular volume of homologous series of similarly branched paraffins, Egloff and Kuder (*J. Physical Chem.*, 1941, **45**, 836) have shown that, at the boiling points, molecular volume can be expressed as a logarithmic function of boiling point. From their formula it may be deduced that the exaltation, or difference from the value for the straight-chain isomer, of the molecular volume for any branched-chain paraffin can be expressed as a function of the exaltation of the boiling point for that isomer. Now the molecular volumes for the normal paraffins, when plotted against molecular weight, lie on smooth curves, both at the boiling points as found by Egloff and Kuder, and also at 20° according to Deanesley and Carleton (*ibid.*, 1941, **45**, 1104; cf. Part I of this series, *J.*, 1950, 2989). It will be seen, however, from Fig. 1 that the exaltations of the boiling point for the branched-chain series, when plotted against molecular weight, undergo an abrupt change of direction at some point between C_5 and C_9, below which the data are discarded by Egloff and Kuder in the derivation of their expression. This change of direction occurs in each case where the chain length increases to five or more carbon atoms, and must be attributed to variations in the potentialities for curling of the carbon chain, because it is already known from our measurements of the solvent-effect constants of the alkyl iodides (*J.*, 1942, 358, Fig. 3) that a marked and definite change takes place in the increments of the solvent-effect constant and hence of the shape of the carbon chain between the fifth and the sixth member of the homologous series. The change of direction beyond a chain length of five carbon atoms will therefore occur between C_5 and C_9 according to the nature of the chain branching, and is not just an anomaly associated with the initial members of the various series. From these considerations it follows that the molecular-volume exaltations at the boiling point may be expected to change direction at the same position in the series, and it is owing to this circumstance that Egloff and Kuder discarded the lower members of the series.

It should also be found that the molecular-volume exaltations at a fixed temperature such as 20° should exhibit a similar change of direction, because the increase of molecular volume between 20° and the boiling point will be related to the (b. p. — 20°) temperature interval, which in passing up the series is subject to the same sharp discontinuity as the exaltations of the boiling point. This sharp change of direction in the molecular volume curves is, in fact, realised experimentally, and is shown in Fig. 2; the shapes of the curves although algebraically inverted are strikingly similar to those in Fig. 1. The change of direction in the various homologous series occurs at precisely the same points for the molecular volume at 20° as for the exaltations of the boiling points.

Egloff and Kuder (*loc. cit.*) found that, at the boiling point, the molecular-volume exaltations are all negative, and for isomeric paraffins fall into the same sequence as that for the change of shape of the molecules from an elongated to a compact structure. On the contrary, the exaltations of the boiling points, Δ b. p., although also negative, are not related to the shape of the structure in the same sequence as the molecular volume (see Table I). The molecular volumes (M/d) of the isomers at 20° fall into a different order from that at the boiling point, because the temperature coefficients of M/d for the various isomers have to be multiplied by the varying number of degrees which depend on the values of Δ b. p. In the case of the seven C_7 isomers considered by Egloff and Kuder (*loc. cit.*) those isomers having relatively small exaltations

FIG. 1.

Exaltation of the boiling points of the branched-chained paraffins.

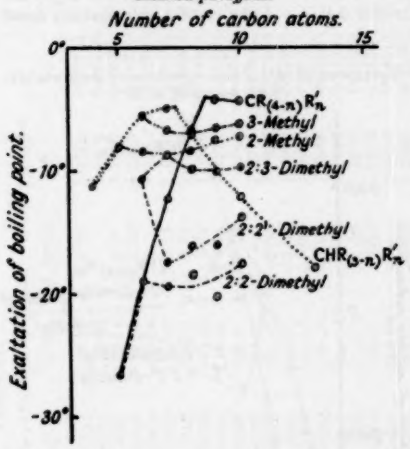


FIG. 2.

Exaltation of the molecular volumes of the branched-chain paraffins at 20°.

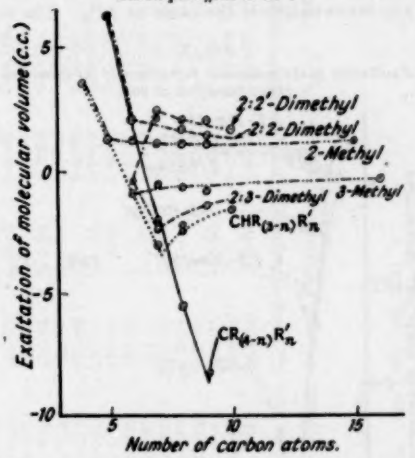


FIG. 1.

The groups represented by R *are as nearly identical as possible* (R′ *is next higher alkyl group to* R): $CHR_{(3-n)}R'_n$ *includes* isobutane, 2-methylbutane, 3-methylpentane, 3-ethylpentane, *etc.* $CR_{(4-n)}R'_n$ *includes* neopentane, 2 : 2-dimethylbutane, 3 : 3-dimethylpentane, 3-ethyl-3-methylpentane, 3 : 3-diethylpentane, *etc.*

of the boiling point move down whilst those with large values of Δ b. p. move up the series of isomers, as indicated by arrows in Table I, to give the molecular volume sequence at 20° with its apparent anomaly that certain isomers have, at 20°, lower densities than the normal paraffin.

TABLE I.

Sequence of molecular volumes and boiling points compared with the molecular shape of C_7 *paraffins.*

Sequence for M/d at b. p.	Molecular shape.	Δ b. p.	Change of sequence.	Sequence for M/d at 20°.
n-Heptane		0°	↘	2 : 4-Dimethylpentane
2-Methylhexane		−8·7	↘	2 : 2-Dimethylpentane
3-Methylhexane		−6·6	↘	2-Methylhexane
2 : 2-Dimethylpentane		−19·5	↗	*n*-Heptane
2 : 4-Dimethylpentane		−17·6	↗	3-Methylhexane
3 : 3-Dimethylpentane		−12·4	↘	2 : 2 : 3-Trimethylbutane
2 : 2 : 3-Trimethylbutane		−17·6	↗	3 : 3-Dimethylpentane

Relationships between Refraction, Total Polarisation, and Boiling Point.—In Part I of this series (*loc. cit.*) it was found that the values of the molecular refraction and total polarisation for the liquid *n*-paraffins can be derived by combining the gas values with the effect of the field

anisotropy, and that all the experimental values can be built up from electron polarisation terms for each kind of bond together with atom polarisation terms for each kind of atom, with in every case a parameter x' corresponding to the contribution of each bond and atom to the shape of the molecule. The observed total polarisation P_S for these compounds is thus made up essentially of three parts:

$$P_S = P_E + P_A + x' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

In a set of isomeric paraffins the same atoms are present in each isomer and consequently P_A should be constant, but as the electron orbits are differently arranged, the mobilities of the electrons will vary, giving different values of P_E. These can be expressed in terms of exaltations ΔP_E which are the amounts by which the electron polarisations of the isomers differ from those of the normal paraffin. Wibaut and Langedijk's data (*Rec. Trav. chim.*, 1940, **59**, 1220) show that the dispersions of isomeric paraffins are identical, so that for any given isomer $\Delta[R]$ for any wave-length is the same as ΔP_E. The exaltation ΔP_{E+A} of the elastic polarisation must

FIG. 3.

Exaltation of the molecular refraction of the branched-chain paraffins at 20°.

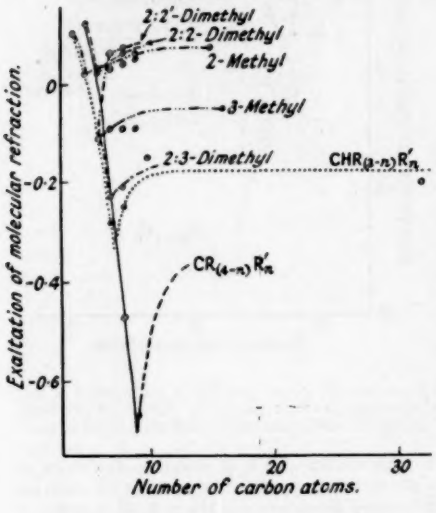
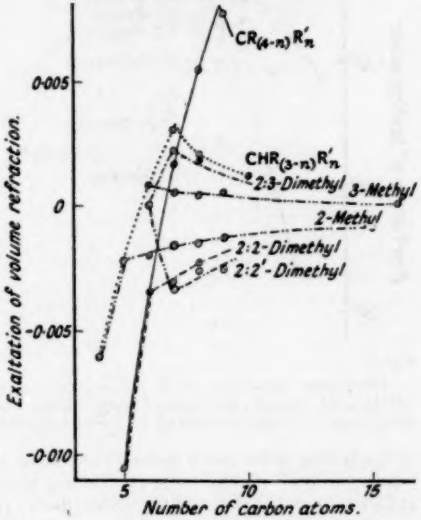


FIG. 4.

Exaltation of the volume refraction of the branched-chain paraffins at 20°.



include ΔP_E, but as P_A should be constant for all the isomers, then for any given paraffin it should be found that

$$\Delta[R] = \Delta P_E = \Delta P_{E+A} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

As these small exaltations depend on the nature of the chain branching it is to be expected that for a *given homologous series* of similarly branched paraffins at the boiling point, $\Delta[R]^{b.p.}$ should be a constant because the value of $[R]^{b.p.}$ would be, as with the normal isomers, a linear function of molecular weight. At 20°, on the other hand, the values of $[R]^{20}$ for the branched-chain paraffins will, just as with the normal isomers, by a suitable modification of formula (1) and as explained in Part I (*loc. cit.*), differ from $[R]^{b.p.}$ by a value for the parameter x' which is dependent on the (b. p. − 20°) intervals. The values of x' for the branched-chain paraffins will be different from those of the corresponding normal isomers owing to their smaller (b. p. −20°) intervals, and this difference between the values of x' must be added to the presumed constant exaltation for the particular homologous series of isomers at the boiling point. The values of $\Delta[R]^{20}$ so obtained, like those of $\Delta(M/d_4^{20})$, when plotted against molecular weight, give curves of similar shape (Fig. 3) to the curves for the exaltation of the boiling point, but tending towards a series of constant values for the higher members. A comparable parallelism between the exaltations of the molecular refraction and of the molecular volume for the liquid

TABLE II.

Physical constants related to the refraction of branched-chain paraffins.

	Ref. no.	Hydrocarbon.	B. p.	Δ b. p.	d_4^{20}.	M/d.	Δ (M/d).	n_D^{20}.	r_D.	Δr_D. × 10^5	$[R]_D$.	Δ$[R]_D$.
C_5.	1.	2-Methylbutane	28·0°	− 8·1°	0·6197	116·42	1·23	1·3539	0·21734	−214	25·30	0·02
	2.	*n*-Pentane	36·1	—	0·6263	115·19	—	1·3578	0·21948	—	25·28	—
C_6.	3.	2 : 2-Dimethylbutane	49·7	−19·0	0·6492	132·74	2·06	1·3688	0·22553	−340	29·94	0·02
	4.	2-Methylpentane	60·2	− 8·5	0·6532	131·92	1·24	1·3715	0·22701	−192	29·95	0·03
	5.	*n*-Hexane	68·7	—	0·6594	130·68	—	1·3750	0·22893	—	29·92	—
	6.	2 : 3-Dimethylbutane	58·0	−10·7	0·6617	130·23	−0·45	1·3750	0·22893	000	29·81	−0·11
	7.	3-Methylpentane	63·2	− 5·5	0·6643	129·72	−0·96	1·3766	0·22979	086	29·81	−0·11
C_7.	8.	2 : 4-Dimethylpentane	80·8	−17·6	0·6728	148·93	2·39	1·3815	0·23245	−337	34·62	0·06
	9.	2 : 2-Dimethylpentane	78·9	−19·5	0·6739	148·68	2·14	1·3822	0·23283	−299	34·62	0·06
	10.	2-Methylhexane	89·7	− 8·7	0·6787	147·63	1·09	1·3849	0·23429	−153	34·59	0·03
	11.	*n*-Heptane	98·4	—	0·6837	146·54	—	1·3877	0·23582	—	34·56	—
	12.	3-Methylhexane	91·8	− 6·6	0·6970	145·85	−0·69	1·3887	0·23635	053	34·47	−0·09
	13.	3 : 3-Dimethylpentane	86·0	−12·4	0·6933	144·52	−2·02	1·3909	0·23753	171	34·33	−0·23
	14.	2 : 3-Dimethylpentane	89·7	− 8·7	0·6951	144·15	−2·39	1·3920	0·23813	231	34·33	−0·23
	15.	3-Ethylpentane	93·3	− 5·1	0·6984	143·47	−3·07	1·3935	0·23893	311	34·28	−0·28
C_8.	16.	2 : 5-Dimethylhexane	109·3	−16·3	0·6941	164·56	2·00	1·3928	0·23856	−255	39·26	0·07
	17.	2 : 2-Dimethylhexane	107·0	−18·6	0·6953	164·28	1·72	1·3935	0·23893	−218	39·25	0·06
	18.	2-Methylheptane	117·2	− 8·4	0·6979	163·67	1·11	1·3949	0·23969	−142	39·23	0·04
	19.	*n*-Octane	125·6	—	0·7026	162·56	—	1·3975	0·24111	—	39·19	—
	20.	3-Methylheptane	119	− 7	0·7058	161·84	−0·72	1·3985	0·24162	051	39·10	−0·09
	21.	2 : 3-Dimethylhexane	115·7	− 9·9	0·7123	160·36	−2·20	1·4012	0·24307	196	38·98	−0·21
	22.	3-Ethylhexane	118·9	− 6·7	0·7136	160·07	−2·49	1·4016	0·24328	217	38·94	−0·25
	23.	3-Methyl-3-ethylpentane	118·4	− 7·2	0·7274	157·03	−5·53	1·4078	0·24659	548	38·72	−0·47
C_9.	24.	2 : 6-Dimethylheptane	134·5	−16·2	0·7098	180·68	1·99	1·3908	0·24285	−246	43·88	0·05
	25.	2-Methyloctane	143·2	− 7·5	0·7134	179·77	1·08	1·4032	0·22413	−118	43·89	0·06
	26.	*n*-Nonane	150·7	—	0·7177	178·69	—	1·4054	0·24531	—	43·83	—
	27.	3-Methyloctane	144·2	− 6·5	0·7210	177·88	−0·81	1·4065	0·24590	059	43·74	−0·09
	28.	3 : 3-Diethylpentane	146·4	− 4·3	0·7524	170·45	−8·24	1·4200	0·25306	775	43·16	−0·67
C_{10}.	29.	*n*-Decane	174·0	—	0·7300	194·88	—	1·4118	0·24872	—	48·47	—
	30.	4-Propylheptane	161·8	−12·2	0·7360	193·31	−1·57	1·4141	0·24994	122	48·32	−0·15
C_{15}.	31.	2-Methyltetradecane	—	—	0·7656	277·44	1·16	1·4304	0·25853	−085	71·73	0·07
	32.	*n*-Pentadecane	—	—	0·7688	276·28	—	1·4320	0·25938	—	71·66	—
C_{16}.	33.	*n*-Hexadecane	—	—	0·7739	292·60	—	1·4347	0·26077	—	76·30	—
	34.	3-Methylpentadecane	—	—	0·7749	292·21	−0·39	1·4350	0·26094	017	76·25	−0·05
C_{22}.	35.	*n*-Dotriacontane	—	—	0·8141	553·80	—	1·4559	0·27178	—	150·51	—
	36.	11-Decyldocosane	—	—	0·8127	554·75	0·95	1·4543	0·27096	−082	150·31	−0·20

Data for *n*-paraffins C_5 to C_{16} are smoothed values from Part I (*loc. cit.*), C_{22} being extrapolated from the series constants calculated from them.

Data for the branched-chain paraffins are:

C_5 to C_8. Concordant values of Wibaut and Langedijk (*loc. cit.*); Forziati, Glasgow, Willingham, and Rossini (*J. Nat. Bur. Stand.*, 1946, **36**, 129); Edgar and Calingaert (*loc. cit.*); and from the present work.

No. 24. Vogel (*J.*, 1946, 133).

Nos. 25 and 27. White and Glasgow (*J. Nat. Bur. Stand.*, 1937, **19**, 423).

No. 28. Horton (*J. Amer. Chem. Soc.*, 1947, **69**, 182).

Nos. 31 and 34. Lunshof, van Steenis, and Waterman (*Rec. Trav. chim.*, 1947, **66**, 348).

No. 36. Whitmore, Sutherland, and Cosby (*J. Amer. Chem. Soc.*, 1942, **64**, 1360).

paraffins has indeed been noted by Edgar and Calingaert (*J. Amer. Chem. Soc.*, 1929, **51**, 1540) although, as may be seen from Table II, their particular method of comparing the effect of chain branching on these properties is only approximately true.

It is to be concluded that the molecular refraction exaltations at the boiling points, like those of the molecular volume, are almost always negative for the paraffins. *iso*Butane is an exception, but this does not invalidate our conclusions in general because the precise values of x' are not known. Boiling-point data are only used as an approximation where gas data are not available (see Part I, *loc. cit.*). This conclusion is confirmed by the values for this apparently exceptional case of *iso*butane which, by extrapolation of the known values for its homologues as shown in Fig. 3, would appear to have a positive $\Delta[R]$ of about 0·1 c.c. and has in fact at its boiling point a $\Delta[R]$ of +0·05 and a $\Delta(M/d)$ of +1·3. Nevertheless, in the gaseous state (Watson and Ramaswamy, *Proc. Roy. Soc.*, 1936, *A*, **156**, 144) *iso*butane has the expected negative exaltation ($\Delta[R] = -0{\cdot}02$). The position of *neo*pentane is similar to that of *iso*butane and the approximate data for both of these hydrocarbons extrapolated to 20° from their recorded constants at low temperatures have beeen included in Figs. 2, 3, and 4, and it will be seen that the points lie on the natural extensions of the appropriate curves.

Since the molecular dimensions $[R]$ and M/d of the various isomers exhibit related exaltations, it follows that the volume refraction [or refraction per c.c., $r = (n^2 - 1)/(n^2 + 2)$], which is also the quotient $[R]/(M/d)$, will give the same characteristic curves with sharp change of direction when the values are plotted against molecular weight as in Fig. 4. The change of direction is seen to occur at the usual positions for the various homologous series. The volume refraction is in many ways the most satisfactory function to employ in the investigation of these hydrocarbon exaltations because it does not include the molecular weight, which in the molecular functions has the arithmetical effect of exaggerating errors of measurement for the higher members of the series, as can be seen by a comparison of Figs. 3 and 4.

Our conclusion that the exaltations of molecular refractions at 20° for homologous series are not constant for the lower members appears to conflict with Wibaut and Langedijk (*loc. cit.*), who find that the increments of molecular refraction for branched-chain series such as those terminated by *iso*propyl or *tert.*-butyl groups are " the same " or " differ but *little* " (their italics) from the increment for the normal paraffin series. It is evident, however, that they do observe differences, especially in the 2 : 3-dimethyl series, because they record, but do not plot, the molecular refraction for 2 : 3-dimethylbutane, which from their viewpoint appears to have an unexpectedly high value, until it is noted that its boiling point is low in comparison with the higher members of the series. As we have already indicated, Wibaut and Langedijk's generalisation for molecular refractions of these series should be strictly true only at the boiling points and especially in the gaseous state. At 20° the variations in the (b. p. − 20°) interval cause the apparent irregularities, but in proceeding higher up the series the boiling points become smoothly related to the molecular weight just as in the series of normal paraffins.

Relationships between Refraction and Total Polarisation, and their Use as Criteria of Purity.— The relationship which we have suggested for the exaltations of the molecular volume and the refraction of the branched-chain paraffins, namely, the dependence on the exaltation of the boiling point, as expressed by curves such as those in Figs. 1—4 found for the various homologous series, can be used to check the structures of paraffins presumed to belong to them and to decide between different values of physical constants recorded in the literature. The purity of the hydrocarbons, irrespective of whether they belong to any particular series, may also be checked by the equivalence (2). For this purpose, a precise knowledge of the true value of $[R]$ is not necessary because, owing to the high dielectric constants of polar impurities, these will cause a large change in ΔP_{E+A} whereas $\Delta[R]$ is only slightly altered. This may be illustrated by measurements which we have made on certain samples of the paraffins enumerated in Table III. We find that if, for a given sample, the relationship $\Delta[R] = \Delta P_{E+A}$ holds true within narrow limits ($\pm 0{\cdot}06$) to include possible inequalities in the respective values of x' as well as errors of experiment, the sample is then found to have a correct value for its density (to within $\pm 0{\cdot}0002$). When, however, the exaltation of the total polarisation is higher than that of the refraction (by more than 0·06), indicating the presence of polar impurities, the density is also in error by a small amount. In the case of these particular compounds the densities and refractive indices for highly purified samples are accurately known, but this is not essential and the method can be successfully applied to new members of the paraffin series for which other constants are not accurately known. Additional help in judging the structure and purity of samples may be obtained from the fact that the molecular volumes must fall into their proper order and, as shown by Edgar and Calingaert (*loc. cit.*), the refractive indices and dielectric constants must fall

approximately into a similar sequence for a given set of isomers. In all, a sensitive test of purity is available, as well as methods for the prediction of the properties of new compounds.

TABLE III.

Equivalence of $\Delta[R]_D$ *and* ΔP_{E+A} *and detection of polar impurities in non-polar* C_7 *and* C_8 *hydrocarbons by comparison of exaltation.*

Sample no.	Hydrocarbon.	$[R]_D$.	P_{E+A}.	$\Delta[R]_D$.	ΔP_{E+A}.	d_4^{20}: lit. val.	d_4^{20}: sample.	Diff. of $\Delta[R]_D$ and ΔP_{E+A}.	Diff. between values of density.
	(A) Properties at 20° of hydrocarbon samples having $\Delta[R]_D = \Delta P_{E+A}$.								
C_7.									
1.	2 : 2-Dimethylpentane	34·62	34·60	0·06	0·09	0·6739	0·6737	0·03	−0·0002
2.	2-Methylhexane	34·59	34·56	0·03	0·05	0·6787	0·6789	0·02	0·0002
3.	*n*-Heptane	34·56	34·51	—	—	—	—	—	—
4.	3-Methylhexane	34·47	34·37	−0·09	−0·14	0·6870	0·6870	−0·05	0
5.	3 : 3-Dimethylpentane	34·33	34·34	−0·23	−0·17	0·6933	0·6934	0·06	0·0001
6.	2 : 3-Dimethylpentane	34·33	34·31	−0·23	−0·20	0·6951	0·6951	0·03	0
7.	3-Ethylpentane	34·28	34·17	−0·28	−0·34	0·6984	0·6984	−0·06	0
C_8.									
8.	2 : 5-Dimethylhexane	39·26	39·19	0·07	0·07	0·6941	0·6941	0	0
9.	*n*-Octane	39·19	39·12	—	—	—	—	—	—
10.	3-Ethylhexane	38·94	38·86	−0·25	−0·26	0·7136	0·7136	−0·01	0
11.	3 : 4-Dimethylhexane	38·87	38·75	−0·32	−0·37	0·7195	0·7195	−0·05	0
12.	2 : 3 : 3-Trimethylpentane	38·77	38·67	−0·42	−0·45	0·7262	0·7262	−0·03	0
13.	3-Ethyl-3-methylpentane...	38·72	38·67	−0·47	−0·45	0·7274	0·7274	0·02	0
	(B) Hydrocarbon samples having high values of ΔP_{E+A} accompanied by high densities.								
C_7.									
14.	2 : 4-Dimethylpentane	34·59	34·91	0·03	0·40	0·6728	0·6733	0·37	0·0005
15.	2 : 3-Dimethylpentane	34·30	34·74	−0·26	0·23	0·6951	0·6956	0·49	0·0005
C_8.									
16.	2 : 2-Dimethylhexane	39·32	39·47	0·13	0·35	0·6953	0·6959	0·24	0·0006
17.	2-Methylheptane	39·26	39·41	0·07	0·29	0·6979	0·6982	0·22	0·0003
18.	3 : 3-Dimethylhexane	38·99	39·11	−0·20	−0·01	0·7100	0·7105	0·19	0·0005
19.	2 : 3 : 4-Trimethylpentane	38·88	38·93	−0·31	−0·19	0·7190	0·7194	0·12	0·0004

The values of $[R]_D$ in Section (A) and the literature values of d are from concordant determinations recorded mainly by Wibaut and Langedijk (*loc. cit.*), Forziati, Glasgow, Willingham, and Rossini (*loc. cit.*), Edgar and Calingaert (*loc. cit.*), and this paper. Values of P_{E+A} in Section (A) are calculated from the literature values of d. In Section (B), both $[R]_D$ and P_{E+A} are from the actual constants of the samples.

Other data for samples 1, 2, 4, 5, and 6 are the values recorded by Smyth and Stoops (*loc. cit.*) after their dielectric constants have been corrected to allow for their method of calibration, using for benzene $\epsilon^{25} = 2·279$. Samples 8 and 11 were prepared for these measurements. Samples 7, 10, and 12—19 inclusive were lent by the Institute of Petroleum Hydrocarbon Bank.

Data for the normal hydrocarbons from Part I of this series (*loc. cit.*) are included for comparison.

Smyth and Stoops (*J. Amer. Chem. Soc.*, 1928, **50**, 1883) concluded from their measurements of the C_7 isomers that P_A appears to change a little in line with the changes in the values of $[R]$ and P_E. However, our criteria of purity being adopted for these hydrocarbons, three of their isomers would be rejected, and any slight fall in P_A for the other five members which are included in Table II would be less than the unavoidable errors. Our measurements for the C_8 isomers show no indication of any regular variation in the value of P_A which, if it occurred, would mean that $\Delta[R]$ would not equal ΔP_{E+A}. The data in Table III indicate that within the limits of probable error P_A is independent of the nature of the chain-branching as was assumed in our derivation of expression (2).

EXPERIMENTAL.

Density, dielectric constant, and temperature were measured as previously described (*J.*, 1940, 893), refractive index by means of an Abbé refractometer.

Preparation and Purification of Materials.—2 : 5-Dimethylhexane was prepared from sodium and *iso*butyl bromide (from Kahlbaum's *iso*butyl alcohol) and impurities were removed by successive washings with sulphuric acid; b. p. 108—109°/750 mm., d_4^{20} 0·69407, n_D^{20} 1·3928, ϵ^{20} 1·9376. 3 : 4-Dimethylhexane was prepared similarly from *sec.*-butyl iodide; b. p. 117·5—118°/750 mm., d_4^{20} 1·71955, n_D^{20} 1·4045, ϵ^{20} 1·9688.

Physical constants of samples lent by the Institute of Petroleum Hydrocarbon Bank were measured without further purification.

		B. p.	d_4^{20}.	n_D^{20}.	c.
C_7.	2 : 4-Dimethylpentane	80·8°	0·67335	1·3815	1·9195
	2 : 3-Dimethylpentane	90·6	0·69557	1·3920	1·9533
	3-Ethylpentane	93·2	0·69837	1·3935	1·9379
C_8.	2 : 2-Dimethylhexane	107·0	0·69587	1·3937	1·9498
	2-Methylheptane	117·2	0·69820	1·3952	1·9519
	3 : 3-Dimethylhexane	111·8	0·71053	1·4000	1·9645
	3-Ethylhexane	118·6	0·71361	1·4014	1·9617
	2 : 3 : 4-Trimethylpentane	113·6	0·71941	1·4043	1·9738
	2 : 3 : 3-Trimethylpentane	114·2	0·72623	1·4076	1·9780
	3-Ethyl-3-methylpentane	118·4	0·72740	1·4078	1·9800

The authors thank the Department of Scientific and Industrial Research and the Research Fund Committee of the Chemical Society for financial assistance. They also thank the Hydrocarbon Research Group of the Institute of Petroleum Research Committee for the loan of hydrocarbons.

THE UNIVERSITY, LEEDS, 2. [*Received, July 6th*, 1950.]

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28. *Some Comments on the B.E.T. (Brunauer–Emmett–Teller) Adsorption Equation.*

By D. C. JONES.

The B.E.T. (Brunauer–Emmett–Teller) adsorption equation is compared with Langmuir's Cases IV and VI. An analysis of the equation leads to corrected conditions for the occurrence of adsorption curves of types II and III. The locus of the points of inflection realisable in type II curves is investigated.

GREAT interest has been aroused in the B.E.T. (Brunauer–Emmett–Teller) equation which was derived by application of the usual Langmuir kinetic method to multimolecular adsorption on a free surface. The theory was then extended in an interesting way to adsorption in capillaries where the diameter of the capillary provided a mechanical obstruction to the development of more than a limited number of adsorbed layers, and also to capillary condensation.

It is, however, often forgotten that Langmuir himself, in his well-known paper (*J. Amer. Chem. Soc.*, 1918, **40**, 1361) visualised and formulated an equation to cover the case of adsorbed films more than one molecule thick, which he labelled Case VI, and in which he made the same assumption which later Brunauer, Emmett, and Teller (Brunauer, "The Adsorption of Gases and Vapours," Oxford Univ. Press, 1945) made in order to arrive at their equations for adsorption on a free surface. The development of the equations differs somewhat, but the same result is obtained although it is expressed in different terms. In the present paper the two methods are briefly compared and a closer study is then made of the form of the theoretical adsorption curves.

Langmuir (*loc. cit.*) showed that the equation obtained for Case VI is identical with that obtained for his Case IV, in which each elementary space is assumed to hold more than one adsorbed molecule and the rate of evaporation is dependent on the number of adsorbed molecules present per elementary space. In Case IV, ν_n represents the rate of evaporation from elementary spaces containing n molecules, α_n is the reflection coefficient corresponding to spaces containing $(n-1)$ molecules and σ_n ($\equiv \alpha_n/\nu_n$) is the corresponding relative life. The development is now as in Langmuir's Case I: when equilibrium is reached the rate of evaporation from that fraction of the surface containing elementary spaces with the same number of molecules is balanced by the rate of condensation in such spaces; the equation obtained at equilibrium is

$$\frac{N}{N_0}\eta = \frac{\sigma_1\mu + 2\sigma_1\sigma_2\mu^2 + 3\sigma_1\sigma_2\sigma_3\mu^3 + \ldots}{1 + \sigma_1\mu + \sigma_1\sigma_2\mu^2 + \sigma_1\sigma_2\sigma_3\mu^3 + \ldots} \quad \ldots\ldots (26)$$

where η is the total quantity of adsorbed gas expressed in g.-mols., N is Avogadro's number, N_0 is the number of elementary spaces per sq. cm., μ is the collision number, and $\sigma_1, \sigma_2 \ldots \sigma_n$ are the relative lives of the adsorbed molecules in the elementary spaces containing 1—n molecules. In Case VI, where multilayers are presumed to occur, ν_n is the rate of evaporation from the nth layer, and α_n the reflection coefficient of molecules striking the $(n-1)$th layer. If we "assume each elementary space holds one molecule only, the problem is then identical with Case IV . . . . and a solution of the problem is given by Eq. 26." Langmuir's treatment

is now to take out σ_1 from the numerator of equation (26) and to divide both numerator and denominator by the numerator; then we have

$$\frac{N}{N_0}\eta_i = \frac{\sigma_1}{(1/\mu) + a + b\mu + c\mu^2 + \ldots} \quad \ldots\ldots\ldots \quad (29)$$

where $a = \sigma_1 - 2\sigma_2$, $b = \sigma_2(4\sigma_2 - 3\sigma_3 - \sigma_1)$, and $c = 2\sigma_2(6\sigma_2\sigma_3 - 2\sigma_3\sigma_4 + \sigma_1\sigma_4 - \sigma_1\sigma_3 - 4\sigma_3^2)$. Now (quoting Langmuir), "if σ_1 and σ_2 are different, but all subsequent values of σ are equal to σ_2, then all coefficients in (29) above b are zero." By making this assumption, which is essentially the same as Brunauer's, it is seen that

$$\frac{N}{N_0}\eta_i = \frac{\sigma_1\mu}{1 + \sigma_1\mu - 2\sigma_2\mu + \sigma_2^2\mu^2 - \sigma_1\sigma_2\mu^2} \quad \ldots\ldots\ldots \quad (30)$$

Equation (30) factorises readily into

$$\frac{N}{N_0}\eta_i = \frac{\sigma_1\mu}{(1 - \sigma_2\mu)[1 + (\sigma_1 - \sigma_2)\mu]} = \frac{1}{1 - \sigma_2\mu} - \frac{1}{1 + (\sigma_1 - \sigma_2)\mu} \quad \ldots \quad (31)$$

$\eta_i N/N_0$ is equivalent to the V/V_m of Brunauer; it is the total adsorption expressed as the number of monolayers.

If one uses the nomenclature of Brunauer and follows the Langmuir method, an expression comparable to (26) is obtained and, after making the Langmuir–Brunauer assumption and dividing algebraically the numerator into the denominator, one obtains the expression (32)

$$\frac{V}{V_m} = \frac{y}{(1 - x)[1 - (x - y)]} = \frac{1}{1 - x} - \frac{1}{1 - (x - y)} \quad \ldots\ldots \quad (32)$$

Comparing equations (32) and (31) it is clear that $y = \sigma_1\mu$, and x or $p/p_0 = \sigma_2\mu$. Brunauer's $c = y/x$ = Langmuir's σ_1/σ_2 or the ratio of the relative lives of the first and subsequent layers. Substituting cx for y in equation (32) we have the Brunauer equation for adsorption on a free surface, *i.e.*,

$$\frac{V}{V_m} = \frac{cx}{(1 - x)[1 - x(1 - c)]} \quad \text{(Brunauer, } op.\ cit.\text{, p. 153).}$$

It should be stated here that Langmuir was of the opinion then that Case VI was operative when (1) the vapour being nearly saturated, the rate of evaporation from the second layer of molecules is comparable with the rate of condensation, and (2) the forces acting between the first and second layers of adsorbed molecules are greater than those holding the first layer to the surface. Langmuir's examination of equation (29) was limited to the statement that "at very low pressures η_i is proportional to μ but at pressures close to saturation η_i begins to increase rapidly and becomes infinite when saturation is reached."

It may be of interest to make some additional analysis of these equations. In general for all ratios of σ_1/σ_2, $\eta_i N/N_0 = 0$ when $\mu = 0$, and $\eta_i N/N_0 = \infty$ when $\mu = 1/\sigma_2$ or $1/(\sigma_2 - \sigma_1)$. The gradient at any point is given by the expression

$$\frac{N}{N_0}\frac{d\eta}{d\mu} = \frac{\sigma_2}{(1 - \sigma_2\mu)^2} - \frac{\sigma_2 - \sigma_1}{[1 - (\sigma_2 - \sigma_1)\mu]^2} \quad \ldots\ldots\ldots \quad (33)$$

and as μ approaches 0, this expression approaches σ_1, or the initial slope at the origin of the adsorption curves ($\eta_i N/N_0$ plotted against $\mu\sigma_2[\mu/\mu_{sat.}]$), is σ_1/σ_2, or on Brunauer's nomenclature, is c (V/V_m plotted against p/p_0). Further

$$\frac{N}{N_0}\frac{d^2\eta_i}{d\mu^2} = \frac{2\sigma_2^2}{(1 - \sigma_2\mu)^3} - \frac{2(\sigma_2 - \sigma_1)^2}{[1 - (\sigma_2 - \sigma_1)\mu]^3}$$

and a point of inflection occurs when

$$\mu = \frac{1 - \left(\frac{\sigma_2 - \sigma_1}{\sigma_2}\right)^{\frac{1}{2}}}{\sigma_2 - \sigma_1 - \sigma_2\left(\frac{\sigma_2 - \sigma_1}{\sigma_2}\right)^{\frac{1}{2}}}$$

or, on Brunauer's nomenclature, when

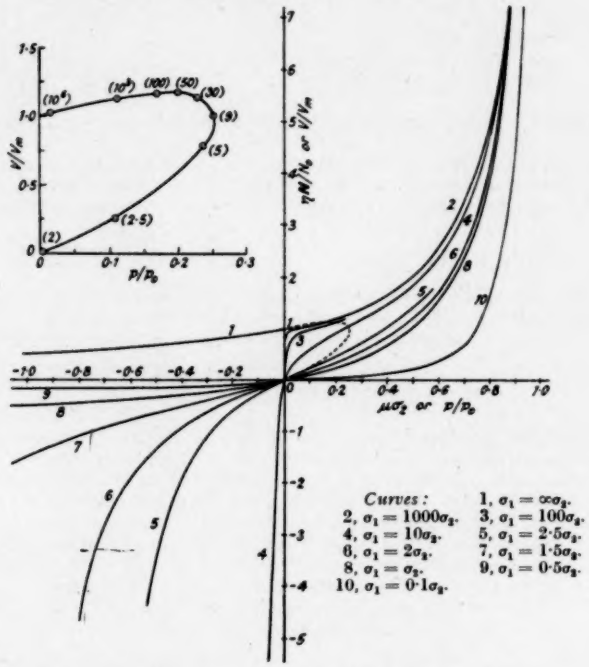
$$\frac{p}{p_0} = \frac{(c - 1)^{\frac{1}{2}} - 1}{(c - 1) + (c - 1)^{\frac{1}{2}}}$$

(*a*) If $\sigma_1 > \sigma_2$:

(1) $\sigma_1 > 2\sigma_2$: the point of inflection occurs at *positive* values of $\mu\sigma_2$ and $\eta_i N/N_0$, the theoretical isotherms being concave to $\mu\sigma_2$ from the origin to the inflection point. This case represents Brunauer's type II, when a sigmoid curve is found experimentally.

(2) $\sigma_1 = 2\sigma_2$: the point of inflection occurs at the origin. In Fig. 1 are arranged typical isotherms calculated for varying ratios of σ_1/σ_2, and the locus of the inflection points is marked as a broken line (see also Fig. 2). It extends from the origin when $\sigma_1/\sigma_2 = 2$, reaches a maximum in respect to μ for $\sigma_1/\sigma_2 = 9$ and then, passing through a maximum in respect to $\eta_i N/N_0$, returns to a value of $\eta_i N/N_0 = 1$ and $\mu = 0$ when $\sigma_1/\sigma_2 = \infty$ ($\sigma_2 \neq 0$).

FIG. 2. FIG. 1.



Point B. This is the point on the isotherm where the middle, flatter portion of the curve begins, and has been used to give the value of V_m. (V_m can also be calculated from the B.E.T. equation.) It is clearly the beginning of the "inflection period," where the previously rapid change of gradient is approaching the point where $\frac{N}{N_0}\frac{d^2\eta}{d\mu^2} = 0$. It may be a help in the fixing of point *B* to know the theoretical inflection point (σ_1/σ_2 or c being known). It would appear from the curves in Fig. 1, that the tendency would be to fix a value of V greater than the real value of V_m if c is greater than 10. Actually if $c = 9$, $\mu\sigma_2 = 0{\cdot}25$ and $\eta_i N/N_0 = 1$, so that the inflection point itself gives the correct monolayer value. If $c > 9$, $\eta_i N/N_0$ has values at the inflection point a little greater (up to 16%) than the correct monolayer value; almost the correct value is given again as c gets very large. If $c < 9$, the inflection point values rapidly fall below the monolayer value for $\eta_i N/N_0$. Theoretically, therefore, and for adsorbents on a free surface, the locus of the inflection points might prove a useful guide in determining which point on the experimental curve gives the best approximation to $V = V_m$; it is clearly not in general "the beginning of the flat portion of the curve." (It may be of value in this connection to investigate, as above, the shape of the theoretical curves when $n \neq \infty$. For certain values of n and c two

points of inflection would be found, the first being near the value of $\eta_i N/N_0$ for $n = \infty$, and the above discussion might be of value in this case also in helping to fix the point where $\eta_i N/N_0 = 1$.)

It is seen from the curves that when σ_1/σ_2 has values close to but greater than 2, the point of inflection approaches the origin, *e.g.*, curve 5 where $\sigma_1/\sigma_2 = 2{\cdot}5$, and it is difficult to detect the sigmoid type in the *experimental* curve where, of course, the part of the curve when η_i and μ have negative values is not available as it is in the *theoretical* isotherms of Fig. 1. The explanation of this difficulty is that when σ_1/σ_2 approaches ∞, the initial gradient approaches $^{\infty}$ and the gradient at the point of inflection approaches 1; as σ_1/σ_2 decreases, so does the initial gradient (σ_1/σ_2), but the gradient at the point of inflection increases until the two gradients become identical and equal to 2 when $\sigma_1/\sigma_2 = 2$ and the point of inflection is at the origin.

The Type II curves of Brunauer are found then when σ_1/σ_2, or c, exceeds 2; the limiting conditions are (1) when $\sigma_1/\sigma_2 = \infty$ $(\sigma_2 \neq 0)$ and (2) when $\sigma_1/\sigma_2 = 2$.

According to Brunauer's approximation that in the expression $c = \frac{a_1}{b_1} \cdot \frac{b_2}{a_2} \cdot e^{(E_1 - E_L)/RT}$, $a_1 b_2$ can be taken without much error as equal to $a_2 b_1$, c becomes $e^{(E_1 - E_L)/RT}$. It is seen that the Type II curve changes over to the Type III, not as usually stated when $E_1 = E_L$ but when $e^{E_1/RT} = 2e^{E_L/RT}$ or, if $T = 300°$, when $E_1 = E_L + 420$ cals. approx.

The case when σ_1/σ_2 has become ∞ $(\sigma_2 \neq 0)$ is interesting. From equation (31) it is seen that in the limit in this case $\eta_i N/N_0 = 1/(1 - \sigma_2\mu)$. This is a hyperbola with asymptotes $\eta_i N/N_0 = 0$ and $\mu = 1/\sigma_2$.* For positive values of $\eta_i N/N_0$ the curve follows closely curve 2 in Fig. 1 from infinity, when $\mu = 1/\sigma_2$, and crosses the ordinate at $\eta_i N/N_0 = 1$; its continuation for negative values of $\mu\sigma_2$ is shown in Fig. 1. This curve represents the further adsorption, according to this model, on an initially complete monolayer.

It will be noted in the theoretical curves of Fig. 1, as is evident from actual adsorption isotherms given in Brunauer's book (*op. cit.*), that for values of μ in the range $0{\cdot}7/\sigma_2$ $(\equiv 0{\cdot}7\ p/p_0)$ upwards, the isotherms would be difficult to detect separately in practice for values of $c > 10$. It should be possible theoretically to determine V_m for such cases, by fitting an experimental curve against this calculated curve for V/V_m against p/p_0 where c is ∞. The calculated curve $(c = \infty)$ would leave the experimental curve at some value of p/p_0, and where it crosses the ordinate would give the value of V which is equal to V_m.

Preliminary calculations show that similar procedures could be used where the adsorption is not on a free surface but where the isotherm is represented by the Brunauer equation (*op. cit.*, p. 154) where $n =$ the number of adsorbed layers that could be fitted into the idealised capillary tube system of an adsorbent.

Another way of making use of this coincidence of the curves at high values of p/p_0 in order to obtain a value for V_m may be illustrated by an example; the theoretical value of V/V_m for $c = \infty$ at a value of p/p_0 of 0·9 is 10; the value of V/V_m that would be observed at the same value of p/p_0 if the experimental curve had a value of $c = 10$ would be 9·9; the value of V_m so calculated from a single adsorption point would thus be 1% low. The error involved in this calculation depends on the value of c.

(*b*) If $1 < \sigma_1/\sigma_2 < 2$: The curves retain their point of inflection, which however now occurs at negative values of $\eta_i N/N_0$ and μ; $\eta_i N/N_0$ as before becomes ∞ at the values of $\mu = 1/\sigma_2$ and $1/(\sigma_2 - \sigma_1)$; *e.g.*, if $\sigma_1 = 1{\cdot}5\sigma_2$, the point of inflection is at $-0{\cdot}327/\sigma_2$ and the curve passes to infinity at $\mu = +1/\sigma_2$ and at $-2/\sigma_2$. As regards the *realisable* part of the adsorption curve this case belongs to the Brunauer Type III.

(*c*) If $\sigma_1 = \sigma_2$: Equation (31) becomes

$$\frac{N}{N_0}\eta_i = \frac{\sigma_2(\sigma_1)\mu}{1 - \sigma_2(\sigma_1)\mu}$$

This again is a hyperbola with asymptotes at $\eta_i N/N_0 = -1$ and $\mu = 1/\sigma_2$ (see curve 8). This represents a limit to the *theoretical* sigmoid curve of Type II, the other limit being the hyperbola obtained when $\sigma_1/\sigma_2 = \infty$. These two hyperbolæ, which represent the limiting cases for theoretical sigmoid adsorption curves on this model, have the same gradients throughout $\frac{N}{N_0}\frac{d\eta}{d\mu} = \frac{\sigma_2}{(1 - \sigma_2\mu)^2}$, and are convex to the abscissa, as an inspection of the second differential shows. Indeed they represent similar adsorption processes: one is the multilayer formation on a completed monolayer whose adsorptive properties are assumed to be equivalent to those

* See also Gregg and Jacobs, *Trans. Faraday Soc.*, 1948, **44**, 577.

of the liquid at the same temperature ($\sigma_2 = \sigma_3 \ldots . \sigma_L$) and the other is the multilayer formation occurring on a surface whose adsorptive properties are equivalent to those of the liquid ($\sigma_1 = \sigma_2$). As has already been pointed out, the *realisable* sigmoid adsorption isotherms have their limit at $\sigma_1 = 2\sigma_2$, when the inflection point has reached the origin. This case (*c*) also belongs to Type III of Brunauer's classification.

It is interesting to compare these cases with the Langmuir Case I (so-called Langmuir adsorption equation), $\frac{N}{N_0}\eta = \frac{\sigma_1\mu}{1+\sigma_1\mu}$. ($\sigma_2 = 0$), which is, of course, also a hyperbola with asymptotes $\eta N/N_0 = 1$ and $\mu = -1/\sigma_1$. This curve is concave to the abscissa for positive values of μ $\left(\frac{N}{N_0}\frac{d^2\eta}{d\mu^2} = \frac{-2\sigma_1^2}{(1+\sigma_1\mu)^3}\right)$. The initial slope ($\mu = 0$) is σ_1 and a monolayer is adsorbed only when $\mu(p) = \infty$; at saturation, ($\mu_{sat.}$ or p_0), the fraction of a monolayer adsorbed is determined by the values of σ_1 and $\mu_{sat.}$ and may be quite small for non-volatile liquids with small values of σ_1. Since $\mu_{sat.}$ is equal to $1/\sigma_2$, this monolayer fraction is determined by the ratio σ_1/σ_L. If the adsorbing surface is of such a kind that $\sigma_1 = \sigma_L$ then at saturation $\eta N/N_0 = 1/2$, as would be the case also for adsorption on the liquid surface itself [the adsorption process is assumed to be limited to a monolayer which is reached (theoretically) at $\mu = \infty$].

(*d*) $\sigma_1 < \sigma_2$ or $0 < c < 1$; *e.g.*, curve 10 when $\sigma_1 = 0{\cdot}1\sigma_2$: Dealing first with the *realisable* portion of the curve, we see that the adsorption is small until considerable values of $\mu\sigma_2$ are reached and that then a steep increase in $\eta N/N_0$ occurs as the curve approaches $\mu = 1/\sigma_2$. Theoretically, after passing through the origin, all curves show a minimum at $p = -p_0/\sqrt{(1-c)}$ and a point of inflection as the curve becomes asymptotic to $\eta N/N_0 = 0$. Beyond the saturation value other, theoretical, portions of the curve occur, with, for example, a maximum appearing at $p = +p_0/\sqrt{(1-c)}$. The *realisable* portion of the isotherm, however, is again of Type III, which therefore is found ranging from $\sigma_1/\sigma_2 = 2$ to $\sigma_1/\sigma_2 =$ a very small value, or when $E_1 = E_L + 420$ cals. (approx.) at room temperature, to $E_1 < E_L$, $E_1 \neq 0$, the previous assumptions holding.

The resemblance between Langmuir's Case VI and the B.E.T. equation for adsorption on a free surface has been pointed out and it has been recalled that the same basic equation holds also for Langmuir's Case IV. Brunauer and his co-workers have made an interesting extension of their theory to cover the case where the adsorption may be limited by the width of the capillary spaces in the adsorbents. The equation covering this case is derived by summing the infinite series in the numerator and denominator of equation (26) to a finite number of terms, the same assumptions being made as before. Both series are of well-known form and can readily be summed to n terms or to infinity. It is clear therefore, and perhaps worth recording, that the same equation is thus obtained as in Langmuir's Case IV where n is the number of molecules per elementary space. The assumption that the relative lives of the adsorbed molecules can be considered equal if $n > 2$ is, perhaps, less plausible here than in the former case. However, this general similarity may partly account for the ability of the Brunauer equation to fit experimental results when the adsorption is a monolayer or less at high values of p/p_0, *e.g.*, the adsorption of iodine on silica gel (Brunauer, *op. cit.*, p. 165). It is intended to make a further analysis of this case later and attention is directed here only to some very general considerations concerning it.

As already pointed out, when $n = \infty$ and for values of $c > 10$ (say), the first layer is almost completed at fairly low values of p/p_0 and, therefore, the parts of the isotherm where p/p_0 have high values are difficult to distinguish; these parts of the isotherm are almost independent of c. This occurs also when n is finite; the value of V/V_m at saturation, now finite, is little affected by the value of c, if $c > 10$. This insensitiveness to the value of c at saturation is diminished by a greater value of n; *e.g.*, if $n = 2$, V/V_m at saturation $= (3/2)(20/21)$ for $c = 10$, $(3/2)(200/201)$ for $c = 100$, and $3/2$ for $c = \infty$; if $n = 6$, the corresponding values are $(7/2)(60/61)$, $(7/2)(600/601)$, and $7/2$. In general, for any values of n, $V/V_m = 0$ when $p/p_0 = 0$, $V/V_m = n$ when $p/p_0 = \infty$, the initial gradient $= c$ and when $p/p_0 = 1$, $V/V_m = [c\eta/(1+c\eta)][(\eta+1)/2]$; this expression approaches $(n+1)/2$ as c approaches ∞.

The author is grateful to Miss E. W. Birks for assistance with some of the calculations.

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29. *Radical Mechanisms in Saturated and Olefinic Systems. Part I. Liquid-phase Reaction of the* tert.*-Butoxy-radical with Olefins and with* cyclo*Hexane.*

By E. H. Farmer and C. G. Moore.

The reactions occurring at 140° between the moderately energetic *tert.*-butoxy-radical and seven hydrocarbons have been studied with the object of determining the characteristic reactivities of the *tert.*-alkoxy-type of organic radical.

The *tert.*-butoxy-radicals, as derived by the thermal scission of di-*tert.*-butyl peroxide, display a reactive tendency towards the non-vinylic olefins and the alkylbenzenes which is practically confined to the dehydrogenation of α-methylene groups, thereby producing olefin radicals which are capable of reacting in the appropriate (isomeric) resonance forms. These olefin radicals do not couple in any significant degree with *tert.*-butoxy-radicals, and hence achieve stabilisation by self-union, giving first dehydro-dimers, then (by the union of dimer radicals with monomer radicals) dehydro-trimers, and subsequently dehydro-tetramers, etc. The stoicheiometrical relation between the peroxide and olefin consumed and the *tert.*-butanol and polymers produced strongly supports the mechanism advanced.

Vinylic (Δ^1-)olefins, as represented by hept-1-ene, possess a dual reactive capacity, being capable of undergoing both ordinary additive polymerisation initiated by radicals and also dehydrogenation and subsequent dehydro-polymerisation like the non-vinylic forms. Hept-1-ene shows both reactivities with *tert.*-butoxy-radicals, the former (leading to essentially saturated polymers) in the higher degree.

Saturated hydrocarbons are attacked by *tert.*-butoxy-radicals at 140°, the secondary $>CH_2$ groupings of *cyclo*hexane being dehydrogenated to yield *cyclo*hexyl radicals, which couple to give di*cyclo*hexyl and thence by further dehydrogenation and coupling higher (mainly saturated) polymers.

The superior capacity for dehydrogenation of tertiary α-methylidyne groupings over secondary methylene, and secondary methylene over primary methyl appears to govern the path of reaction in the case of all unsaturated hydrocarbons, except where steric effects obtrude; and a similar reactivity sequence applies at a lower level to the groupings of saturated hydrocarbons.

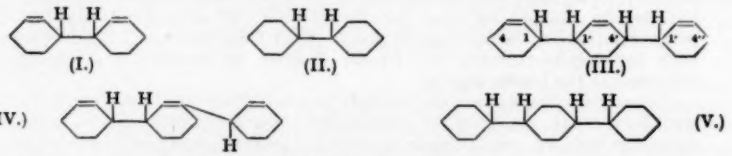
In the present series of papers it will be indicated that differently constituted free readicals show considerable differences in reaction capacity towards olefins in the exercise of the two main reactivities (substitution and addition) open to them. Most radicals seem to be capable of initiating olefinic substitution reactions by detaching α-methylenic hydrogen atoms, but relatively few—and these the more energetic ones—are able to add to the double bond of non-vinylic mono-olefins. Since in the thermal decomposition of hydroperoxides two kinds of radical are produced ($ROOH \longrightarrow RO\cdot + \cdot OH$) whereas in that of *s*-dialkyl peroxides only one kind is produced ($ROOR \longrightarrow 2RO\cdot$), there was good reason, when embarking on the investigation of radical reactivity, to choose first *s*-dialkyl peroxides as radical sources. Also there was good reason to select for the first studies the easily derived and manipulated *tert.*-butoxy-radical, although of course the experimentally convenient properties have as their counterpart a reactivity of only moderately energetic character. This moderately energetic reactivity has proved, however, to lead to very characteristic results and these will be contrasted in subsequent papers with the results accruing from the employment of more reactive radicals such as ·OH.

Di-*tert.*-butyl peroxide breaks down reasonably rapidly above 100°, and for present purposes the temperature of 140° has been selected as suitable both for the generation of radicals and for the attack of the radicals on the olefinic reagent. The peroxide and the various hydrocarbons in turn were heated together in the absence of oxygen in glass Carius tubes for periods varying from 12 to 48 hours. The relative proportions of peroxide to olefin, and the reaction time, were varied somewhat in different experiments, and the effect of the variations on the yield and nature of the reaction products determined.

Reaction with cyclo*Hexene.*—It was desirable for stoicheiometrical reasons to make the quantity of peroxide employed the basis for all calculations of reaction yields. To ensure that all the radicals produced had an opportunity for reaction (with olefins), and correspondingly to minimise any tendency towards their explosive degradation, a large excess of the olefinic reactant was always used.

Reaction of di-*tert.*-butyl peroxide and *cyclo*hexene in the molar ratio of 1 : 6 for 24 or 48 hours resulted in complete decomposition of the peroxide, which was converted mainly into *tert.*-butanol and to a minor extent into acetone. In addition to recovered *cyclo*hexene, a mixture of *cyclo*hexene " polymers " was obtained which contained no oxygenated constituents. By fractional distillation of the " polymer " mixture there were obtained three well-defined fractions, a " dimer " $C_{12}H_{18}$, a " trimer " $C_{18}H_{26}$, and a " tetramer " $C_{24}H_{34}$; above this, a mixture of higher " polymers " remained which were capable of distillation only in high vacuum. These products were clearly dehydropolymers, and not true polymers $(C_6H_{10})_n$; for convenience, however, in the following account the unqualified terms dimer, trimer, polymer, etc., are used to signify these dehydro-forms except where it is otherwise made clear.

The dimer, $C_{12}H_{18}$. This proved to consist entirely of the dicyclic diolefin, di*cyclo*hex-2-enyl (I). The presence of two double bonds per C_{12} unit was confirmed both by iodine-value determinations and by catalytic hydrogenation. The tetrahydride derived by hydrogenation was pure di*cyclo*hexyl (II); furthermore, the corresponding saturated bromine-adduct consisted wholly of the two known (doubtless stereoisomeric) tetrabromides, $C_{12}H_{18}Br_4$, of m. p.s 159—160° and 188—190° (cf. Berlande, *Compt. rend.*, 1941, **213**, 484; Farmer and Michael, *J.*, 1942, 513). The dimer itself agreed in its physical constants with synthetic di*cyclo*hex-2-enyl derived by the action of magnesium on 3-bromo*cyclo*hexene.



The trimer, $C_{18}H_{26}$. The trimeric fraction consisted of two isomeric ter*cyclo*hexenyls, (III) and (IV),* and gave on hydrogenation a mixture of the corresponding hexahydrides, $C_{18}H_{32}$. One of these hexahydrides, the already known form of m. p. 162—163°, crystallised out, but about two-thirds of the mixture consisted of uncrystallised structural and stereo-isomers. On dehydrogenation with selenium the trimer gave a mixture of *p*- and *m*-terphenyl, and on treatment with bromine it gave a mixture of difficultly separable hexabromides, only three of which were isolated in substantially pure form. The apparently complete absence of *o*-terphenyl from the dehydrogenation product is significant in relation to the correctness of the mechanism advanced below.

The tetramer, $C_{24}H_{34}$. Many structural and stereo-forms were doubtless present in this polymer, and the only examination undertaken was that required to establish its tetraolefinic dehydro-constitution.

Mechanism of Reaction.—It is seen from the foregoing results that the di-*tert.*-butyl peroxide, when decomposed in *cyclo*hexene, is transformed almost quantitatively into *tert.*-butanol and that those *cyclo*hexene molecules which suffer attack become converted into a mixture of dehydropolymers *without loss of any of the original unsaturation.*

The mechanism advanced to explain these results involves initial homolytic scission of the O–O bond in the peroxide to give two *tert.*-butoxy-radicals. The latter stabilise themselves by abstracting hydrogen atoms from the α-methylene groups of *cyclo*hexene molecules with which they collide favourably, so yielding *tert.*-butanol and a *cyclo*hexenyl radical (cf. Farmer and Michael, *loc. cit.*):

$$C_6H_{10} + Bu^tO\cdot \longrightarrow C_6H_9\cdot + Bu^tOH$$

The existence of traces of acetone in these decompositions suggests that the peroxide undergoes, to a minor extent, unimolecular radical decomposition in a manner analogous to the vapour-phase pyrolysis of the peroxide in the absence of solvents as observed by Milas and Surgenor (*J. Amer.*

* The position of the double bond assigned in the middle ring of (IV) is not easily demonstrable, but is that required for consistency with other observations.

Chem. Soc., 1946, **68**, 205, 643; see also Milas and Perry, *ibid.*, p. 1938), and by Raley, Rust, and Vaughan (*ibid.*, 1948, **70**, 88):

$$Me_3C{\cdot}OO{\cdot}CMe_3 \longrightarrow 2Me_2C{-}O{\cdot} \longrightarrow 2COMe_2 + 2CH_3{\cdot}$$

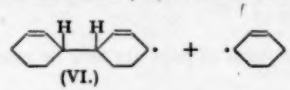
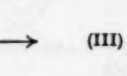
The *cyclo*hexenyl radicals produced by the dehydrogenative action of *tert.*-butoxy-radicals may be expected to become stabilised by the radical–radical coupling reaction (*a*) to give the dimer (I). This process will undoubtedly have a low energy of activation, whereas (the alternative) radical stabilisation by the substitution reaction (*b*) seems from energy considerations to be unlikely to occur. It should be noted that the monomer radical may also participate to some extent in a hydrogen-transfer process (*c*), and in fact spectrographic evidence shows that this type of reaction definitely occurs when the *tert.*-peroxide is thermally decomposed in the presence of hept-1-ene (p. 135) or of 4-methylhept-3-ene (see Part II).

(*a*) $2C_6H_9{\cdot} \longrightarrow C_6H_9{-}C_6H_9$ (I.) (*b*) $C_6H_9{\cdot} + C_6H_{10} \longrightarrow C_6H_9{-}C_6H_9 + H{\cdot}$

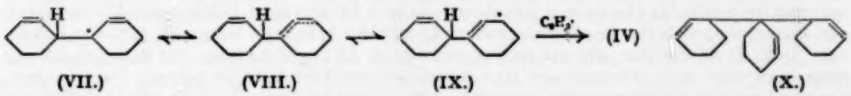
(*c*) $C_6H_9{\cdot} + RH \longrightarrow C_6H_{10} + R{\cdot}$ [RH = olefin molecule; R = alkenyl radical]

It is especially to be noted that the total absence of oxygenated components from the mixture of *cyclo*hexene polymers demonstrates the highly specific reactivity of *tert.*-butoxy-radicals under the present reaction conditions. The latter radicals are obviously mainly limited in their reactivity to hydrogen abstraction from olefinic α-methylene groups, so showing *negligible additive reactivity towards double bonds* ($RO{\cdot} + C{=}C \longrightarrow RO{-}C{-}C{\cdot}$), and *negligible direct substitutive replacements at α-methylene groups* ($RO{\cdot} + {-}CH_2{-}C{=}C{-} \longrightarrow RO{-}\underset{|}{C}H{-}C{=}C + H{\cdot}$).

Turning now to the production of trimeric and higher products, the same basic concepts serve as a basis for formulating the further paths of reaction. The dimer molecules of di*cyclo*hexenyl will, as they are formed in increasing numbers, inevitably compete with the monomer olefin molecules for reaction with *tert.*-butoxy-radicals, and thus they will give *tert.*-butanol and di*cyclo*hexenyl radicals, the latter subsequently giving, by radical–radical unions comparable with (*a*), trimeric, and occasionally tetrameric products. Thus, for the production of (III), the radical coupling of the dimer radical (VI) with the monomer-radical as in (*d*) may be formulated.

(*d*)  (VI.)  (III)

Here, however, some consideration of possibilities is needed. Clearly, radical attack at one or other of the tertiary (inner) α-methylidyne groups of the dimer (to give VII) is likely, in the absence of special circumstances, greatly to outweigh that at one or other of the two secondary (outer) α-methylene groups (to give VI): it is likely, however, that special circumstances will be present, in that the approach of rather large *tert.*-butoxy- or olefin radicals to the inner α-methylidyne carbon atoms may be to some extent sterically hindered, so causing enhancement



(VII.) (VIII.) (IX.) (X.)

of the otherwise relatively unimportant degree of outer-carbon (secondary) α-methylenic attack. Since, in practice, the yield of stereoisomers of (III) amounts to as much as 33% (and possibly a little more) of the trimer fraction, the steric approach factor does, indeed, seem to have a material effect in enhancing substitution at the outer α-methylenic positions by hindering abstraction of hydrogen at the inner ones. But this is apparently not the only result of steric hindrance in affecting reaction of the inner positions, since the predominant substitution of the dimer molecule is found to occur, not just simply at either the inner or the outer positions, but at what appears at first sight to be one of the original (outer) ethylenic carbon atoms (to give IV). This substitutive effect may easily be interpreted as a direct consequence of resonance in the allylic system of the dehydro-dimer radical (VII), the mesomeric form (VIII) of which is impelled, largely by steric hindrance, to react predominantly *via* its radical form (IX). The relatively large-scale operations needed for the confirmation of the presence in very small proportions of the trimer isomer (X), derived from (VII) in the trimer fraction, could not be undertaken.

Below the trimeric stage of aggregation, branching in the polymer chain cannot occur; but

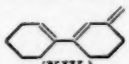
it is noteworthy that it appears as soon as circumstances permit. With the tetrameric and higher polymers the number of structurally-different branched forms may be expected to increase substantially owing to increase in the number of *tert.*-α-methylidyne groups, and simultaneously the number of stereoisomers of both branched and unbranched forms is likely to become rapidly larger.

Conjugation in High Polymers.—A further interesting feature of the correspondence between allylic theory and experimental observation is the appearance of conjugation as soon as it become possible theoretically. For instance, whereas no conjugation is to be observed in the dimer and trimer fractions of radical-polymerised *cyclo*hexene, yet it occurs, and its extent can be measured, in the tetramer, hexamer, etc., fractions. The measurements (see p. 139) permit the deductions that (1) the appearance of two double bonds in one ring is in practice precluded, and (2) the absorption which is to be observed at $\lambda_{max.}$ 2430 A. may be due to either (or both) of the two conjugated diene systems (XI) and (XII) (cf. Booker, Evans, and Gillam, *J.*, 1940, 1453;

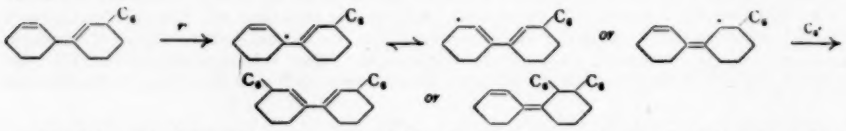
(XI.)

(XII.)

(XIII.)


(XIV.)

Woodward, *J. Amer. Chem. Soc.*, 1942, **64**, 72), the total occurrence of which is of the order of <5% in the tetramer and 10—20% in the hexamer and heptamer–octamer fractions. An unresolved band at $\lambda_{max.}$ 2860 A. may * be due to relatively small amounts of conjugated trienes containing the systems (XIII) and (XIV), which give selective absorption at $\lambda_{max.}$ ~2800 A. (Koch, *Chem. and Ind.*, 1942, **61**, 273). Of course, such conjugation is to be expected theoretically as the outcome of allylic resonance during the conversion of a trimer into a tetramer. This is seen in the following scheme in which the branching *cyclo*hexenyl groups are represented by C_6:



Stoicheiometrical Considerations.—The yields of products may be represented as dependent on the basic equations:

(i) $2C_6H_{10} + ROOR \longrightarrow C_{12}H_{18} + 2R{\cdot}OH$
(ii) $3C_6H_{10} + 2ROOR \longrightarrow C_{18}H_{26} + 4R{\cdot}OH$
(iii) $4C_6H_{10} + 3ROOR \longrightarrow C_{24}H_{34} + 6R{\cdot}OH$ (etc.)

By using these equations, the yields of *tert.*-butanol (R·OH) and *cyclo*hexene polymers formed in the reaction have been correlated with the amount of peroxide decomposed. The correspondence between the observed peroxide expenditure and the total peroxide theoretically required for producing the various polymers is, as may be seen from Tables I and II, very good, and strongly supports the reaction mechanism advanced. It is to be noted that in the 1 : 6 molar run (Table I) all the peroxide has reacted after 24 or 48 hours' heating, but decomposition is incomplete after only 12 hours; also that the relative proportions of the polymer fractions have remained constant in experiments conducted with a constant peroxide/olefin ratio but different reaction times. Comparison of Tables I and II reveals that variation in the peroxide/olefin ratio causes a great difference in the relative yields of the individual polymers; *e.g.*, in the 1 : 6-molar run the polymer yields are of the order dimer 8, trimer 2·7, tetramer 1, whereas in the 1 : 2-molar run the order has changed to dimer 1·75, trimer 1·1, tetramer 1·0.

The relative yields of the different polymeric grades provide further illustration of the different susceptibility to radical attack of primary, secondary, and tertiary C–H bonds. On a statistical basis high yields of trimer and the higher polymers would not be expected, since the peroxide undergoes decomposition in a large excess of olefin, so that the monomeric olefin molecules will always be more abundant than the dimer molecules, and might therefore be expected to react preferentially with the peroxide. The relative susceptibility to attack, however, declines so considerably in the direction C^t–H > C^s–H > C^p–H, that this factor

* Conjugated dienones also absorb at $\lambda_{max.}$ 2690—3170 A., the precise value being dependent on the character of the alkyl substituents, so the observed spectrographic value is not completely conclusive of triene conjugation.

counterbalances the collision-frequency factor sufficiently to have a very pronounced effect on the higher-polymer yields.

TABLE I.

*Reaction of di-*tert.*-butyl peroxide* * *with* cyclo*hexene*.† (Temp. 140°; molar ratio 1 : 6.)

Heating period :	12 Hours.			24 Hours.			48 Hours.		
Products.	Wt., g.	Total polymer, %.	Peroxide acctd. for, %.§	Wt., g.	Total polymer, %.	Peroxide acctd. for, %.§	Wt., g.	Total polymer, %.	Peroxide acctd. for, %.§
tert.-Butanol	43·0	—	87·25	47·4	—	96·2	46·0	—	93·3
Total polymer mixture	42·0	(25·6% *cyclo*hexene)		45·5	(27·75% *cyclo*hexene)		45·0	(27·45% *cyclo*hexene)	
Dimer	25·8	61·45	47·75	28·15	61·85	52·1	27·0	60·45	50·35
Trimer	8·8	20·95	21·8	9·5	20·9	23·55	9·75	21·75	24·2
Tetramer	3·3	7·85	9·2	3·55	7·8	9·9	3·5	7·8	9·8
Higher polymers ‡	3·8	9·05	11·8	3·85	8·45	11·95	4·2	9·3	13·05
Total	—	99·3	90·55	—	99·0	97·5	—	99·3	97·4

* Weight taken, 48·7 g. † Weight taken, 164·0 g. ‡ Assumed to be (on average) hexamer.
§ Owing to the distillation technique used, the various polymer fractions isolated could not be quite pure molecular-weight species but would contain small amounts of the next higher—and lower—polymers. This, of course, introduces slight inaccuracies into the peroxide-equivalence values as given.

TABLE II.

*Reaction of di-*tert.*-butyl peroxide with* cyclo*hexene*. (Temp. 140°; heating period 24 hours.)

	Molar ratio 1 : 4.*			Molar ratio 1 : 2.†		
Products.	Wt., g.	Total polymer, %.	Peroxide acctd. for, %.	Wt., g.	Total polymer, %.	Peroxide acctd. for, %.
tert.-Butanol	46·3	—	93·9	46·0	—	93·3
Total polymer mixture ...	44·4	(40·6% *cyclo*hexene)		35·8	(65·5% *cyclo*hexene)	
Dimer	20·4	45·95	37·75	7·14	19·95	13·2
Trimer	9·5	21·4	23·55	4·56	12·75	11·3
Tetramer	4·6 (*a*)	10·35	12·85	4·1	11·45	11·45
Higher polymers	8·0 (*b*)	18·0	24·9	18·7 (*c*)	52·25	59·85–61·1
Total	—	95·7	99·05	—	96·4	95·8—97·05

* Weights taken : peroxide 48·7 g., *cyclo*hexene 109·3 g.
† Weights taken : peroxide 48·7 g., *cyclo*hexene 54·65 g.

(*a*) Tetramer sample (A) (p. 140). (*b*) Polymer sample (B), average composition hexameric [Found : *M* (in benzene), 470. Calc. for $C_{36}H_{60}$: *M*, 482) (p. 140)]. (*c*) Polymer sample (C), average composition between heptamer and octamer [Found : C, 89·55; H, 10·25%; *M* (in benzene), 605, 615. $C_{42}H_{68}$ requires C, 89·6; H, 10·4%; *M*, 562. $C_{48}H_{68}$ requires C, 89·65; H, 10·35%; *M*, 642) (p. 140)].

Reaction with Dicyclohexenyl.—When the peroxide and olefin reacted together in the molar ratio of 1 : 2 for 48 hours at 140°, all the peroxide decomposed, yielding *tert.*-butanol (92% of theoretical yield isolated). Of particular significance were the facts: (1) that 35·8% of the olefin was recovered unchanged, (2) that 18·5% of the olefin was converted into quater*cyclo*hexenyl, $C_{24}H_{34}$ $\overline{4}$, and (3) that 40·75% of the olefin was converted into a mixture of undistillable polymers having an average composition corresponding to the octamer $C_{48}H_{66}$ $\overline{8}$. These results confirm earlier findings that the radical-coupling procedure is not confined to the first or dimerisation stage of polymerisation engendered by radical–olefin interaction ($2RH \xrightarrow[(-2H\cdot)]{2r\cdot} 2R\cdot \longrightarrow R{-}R$). Here sufficient *tert.*-butoxy-radicals were available to convert all the C_{12} olefin molecules taken into the C_{24} dimer; but, in practice, a third of the monomer molecules escaped attack, and a corresponding proportion of *tert.*-butoxy-radicals became available for hydrogen-abstraction, leading to higher polymer formation.

*Reaction with Hept-*1*-ene.*—Considerable interest attached to the behaviour of the *tert.*-butoxy-radical towards a typical Δ^1- or vinylic mono-olefin since olefins of this groups possess in common a strong tendency towards additive polymerisation, the initial step consisting in the addition of a radical (and a wide range of radicals appear to be effective) to one end of the double bond of a monomer molecule—a tendency, which, as seen above, appears to be wholly replaced by a hydrogen-abstraction tendency in the case of non-vinylic mono-olefins.

When the di-*tert.*-butyl peroxide was heated at 140° with hept-1-ene in the molar ratio of

1 : 4, 85·5% of the peroxide passed into *tert.*-butanol and only a small proportion (6·35%) of the heptene was recovered. The bulk of the olefin had been converted into polymeric materials, the fractionation of which gave three heptene dehydro-dimers A, B, and C, containing traces of oxygenated constituents, together with a large proportion (equivalent to *ca.* 76% of olefin taken) of an undistillable polymer having on average a hexameric composition. The three dimer fractions and the polymer residue all showed a considerably lower degree of unsaturation (as revealed by quantitative catalytic hydrogenation, C/H ratios, and infra-red spectrography) than that appropriate to the original hept-1-ene.

Infra-red spectrographic analysis showed that the recovered portion of the heptene employed now contained distinct traces of unsaturation of type R—CH=CH—R; also the three dimer and the higher-polymer fractions all showed a considerable proportion of the latter type of unsaturation in addition to the original vinylic unsaturation. Absorption bands consistent with the presence of small amounts of ether groups and possibly traces of carbonyl groups also characterised the dimer fractions.

The main conclusions to be drawn from these results are: (1) Much of the peroxide decomposes to give *tert.*-butanol. (2) Extensive polymerisation of the olefin is promoted, but there is a complete lack of correspondence between the relative proportions of recovered heptene, dimer fractions, and higher polymer obtained in this case compared with those obtained in all other cases of non-vinylic mono-olefins examined. (3) The polymers show a significant decrease in unsaturation and an extensive rearrangement of the original vinylic unsaturation. (4) It is to be inferred that two different types of polymerisation are being effected side by side by the action of the *tert.*-butoxy-radicals, *viz.*, (*a*) radical-linking at α-methylenic carbon atoms to give dehydro-polymers of the type described above,* and (*b*) true additive polymerisation of the type well known in the peroxide-catalysed production of high polymeric materials from innumerable vinylic olefins, and terminated by one or other of the usual methods involving disproportionation, radical coupling, or hydrogen abstraction from external molecules.

$$2r\cdot + 2\text{-}CH_2\text{-}C{=}C\text{-} \longrightarrow 2\,r\text{-}H + \begin{matrix}\text{-}CH\text{-}C{=}C\\ |\\ \text{-}CH\text{-}C{=}C\end{matrix} \qquad r\cdot + C{=}C\text{-}R \longrightarrow r\text{-}C\text{-}\dot{C}\text{-}R \xrightarrow{n\,C=CR} r\text{-}(C\text{-}CR_{n+1})\cdot$$

Type (a) [r = Bu^tO] *Type* (b)

The true additive polymerisation reactions of type (*b*), of course, entail substantial loss of original olefinic unsaturation, and the fact that the major product is a nearly saturated polymer of fairly high molecular weight indicates that these reactions compete very favourably with those of type (*a*). The appearance of non-vinylic unsaturation in the monomeric and polymeric reaction products is doubtless due in the main † to resonance in the allylic radical systems produced by hydrogen abstraction, whereby radicals $R\text{-}\dot{C}H\text{-}CH{=}CH_2$ pass extensively into their counterparts, $R\text{-}CH{=}CH\text{-}CH_2\cdot$, before undergoing mutual coupling or each regaining a hydrogen atom. It is of especial interest that some hept-1-ene molecules change their unsaturation in this way, so illustrating the occurrence of exchange reactions between heptene radicals and heptene molecules ($R\text{-}\dot{C}H\text{-}CH{=}CH_2 \rightleftharpoons R\text{-}CH{=}CH\text{-}\dot{C}H_2\cdot \xrightarrow{R\text{-}CH_2\text{-}CH=CH_2}$ $R\text{-}CH{=}CH\text{-}CH_3 + R\text{-}\dot{C}H\text{-}CH{=}CH_2$). Also, it is to be noted that, although all the non-vinylic olefins examined (including those discussed later) tend fairly completely to give the dehydro-type of polymer with *tert.*-butoxy-radicals, yet this representative example of the vinylic type of olefin is able to give, under conditions of reaction which provide an abundance of *tert.*-butoxy-radicals, an appreciable proportion of dehydropolymerisation alongside the predominant additive polymerisation.

Reaction with Alkylbenzenes.—As might be expected, *tert.*-butoxy-radicals attack alkylbenzenes with moderate facility, the aryl nucleus acting as olefinic activating group to the α-methylenic carbon atom in the side chain, and the alkyl group(s) attached to the latter (if any) as subsidiary activating groups ($Ar \curvearrowright CH_2 \leftarrow R$). Thus when di-*tert.*-butyl peroxide is decomposed at 140° in presence of toluene, there are formed dibenzyl and substituted dibenzyls, the latter representing dehydro-trimers, -tetramers, etc., of toluene. Likewise, at the same temperature, the peroxide gives with ethylbenzene a mixture of *meso*- and racemic 2 : 3-diphenylbutanes, CHMePh·CHMePh, together with dehydro-trimers, etc., but with

* To a very minor extent coupling of olefin and butoxy-radicals occurs to give ethers, as revealed by infra-red spectrography.

† Possibly chain-stopping hydrogen-rejections are to some extent responsible ($r\text{-}[CH_2\text{-}CH\text{-}R]_n\cdot \longrightarrow r\text{-}[CH_2\text{-}CH\text{-}R]_{n-1}\text{-}CH{=}CHR$).

*iso*propylbenzene it yields only the homogeneous dimer, 2 : 3-dimethyl-2 : 3-diphenylbutane, $CMe_2Ph{\cdot}CMe_2Ph$,* and no higher polymers.

The approximate yields of polymeric products obtained at 140° from the three alkylbenzenes are given in Table III. The production of a single product from *iso*propylbenzene is to be expected, since only one α-methylenic C–H bond (but that a tertiary one) is present in the monomer, and none at all in the dimer; in contrast, the considerable proportion of trimer and tetramer formed from toluene is doubtless to be attributed to the reactivity of the secondary, and secondary and tertiary α-methylenic C–H bonds present respectively in the dimeric and trimeric products. As regards comparison of the influence of the primary, secondary, and tertiary α-methylenic C–H bonds characterising the three alkylbenzenes (respectively) in promoting reaction with the peroxidic reagent, no valid deduction is to be drawn from the values in Table III; and, indeed, in respect of such relative reactivity it should be mentioned that contemporaneous kinetic studies by Raley *et al.* (*loc. cit.*) on the liquid-phase decomposition of di-*tert.*-butyl peroxide in solvents of widely varying chemical character demonstrate that the rate-determining step in all cases is the unimolecular scission of the peroxidic O–O bond, since the variation in the first-order rates of decomposition is but small.

TABLE III.

Yield (%) *of products at* 140°.*

	Toluene (sealed tube) (24 hours).	Ethylbenzene (atm. press.) (24 hours).	*iso*Propylbenzene (atm. press.) (46 hours).	*iso*Propylbenzene (sealed tube) (24 hours).
Monomer (recovered)	39	69	57	14·5
Dimer	20	26	43	85·5
Trimer	10	5	—	—
Higher polymer	31	5	—	—

* In all these examples, except that of *iso*propylbenzene in the experiment at atmospheric pressure, a 100% excess of hydrocarbon (not taken into account in calculating yields) was employed above that required for a 2 : 1 molar hydrocarbon/peroxide ratio.

It is very noticeable in these experiments with alkylbenzenes that the thermal decomposition of the *tert.*-butoxy-radical (to give acetone) which in the case of simple olefinic hydrocarbons competes very unfavourably with the hydrogen-abstraction function, is considerably enhanced, accounting, for example, in the case of toluene for the very significant proportion of *ca.* 8% of the peroxide consumed.

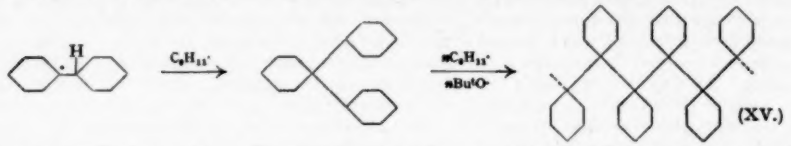
Reaction with cyclo*Hexane.*—Qualitative tests with saturated hydrocarbons showed that decomposing di-*tert.*-butyl peroxide exercised a similar " polymerising " action to that observed with non-vinylic olefins. As an example of such reaction within the group of saturated hydrocarbons, that with *cyclo*hexane was selected since at the monomeric stage all the methylene groups are secondary and equivalent. This hydrocarbon, taken in large excess, was heated for 24 hours at 140° with the peroxide, the products comprising much *tert.*-butanol (92·5% yield), traces of acetone, and a mixture of hydrocarbon polymers with unchanged *cyclo*hexane. Di*cyclo*hexyl formed 22·6% of the polymer mixture, and ter*cyclo*hexyl, $C_{18}H_{32}$ (probably a mixture of isomers), a very much smaller fraction. The major portion of the product (*ca.* 52%) was an orange polymeric residue, essentially of hydrocarbon character, containing apparently an average of 7—8 *cyclo*hexane units per molecule (*M*, 630). This polymer, on spectrographic analysis, showed some unsaturation, including, apparently, *cyclo*hexadiene groupings; but quantitative determination of the unsaturation, or the gaining of evidence as to the extent of its appearance in conjugated diene groups, was frustrated by the insolubility of the polymer.

The large yield of *tert.*-butanol and the substantial amount of di*cyclo*hexyl suggest that reaction followed a similar course to that discussed above for olefins :

$$\text{(i)}\quad Bu^tOOBu^t \longrightarrow 2Bu^tO\cdot;$$
$$\text{(ii)}\quad Bu^tO\cdot + C_6H_{12} \longrightarrow Bu^tOH + C_6H_{11}\cdot;$$
$$\text{(iii)}\quad 2C_6H_{11}\cdot \longrightarrow C_6H_{11}{-}C_6H_{11}$$

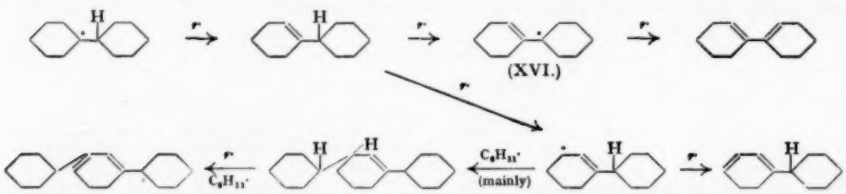
* Kharasch *et al.* (*J. Org. Chem.*, 1945, **10**, 401) have demonstrated the formation of the two 2 : 3-diphenylbutanes from ethylbenzene and dimethyldiphenylbutane from *iso*propylbenzene by the action of radicals from decomposing diacetyl peroxide. Since our experiments were completed, Raley, Rust, Seubold, and Vaughan (*J. Amer. Chem. Soc.*, 1948, **70**, 88, 95, 1336) have reported observations concerning di-*tert.*-butyl peroxide and toluene and *iso*propylbenzene similar to those described here.

The main point of interest in this case is that dehydro-polymerisation beyond the dimeric stage involves selection of the point of dehydrogenative attack between tertiary $\gtrless$CH and (numerous) secondary $>CH_2$ groupings; and if such selection meticulously favours attack at the former (which probably is not quite the case) then reaction must pass through the stages:



(XV.)

except to the extent that a subsidiary procedure for the stabilisation of cyclic hydrocarbon radicals occurs, involving a second dehydrogenation step (immediately following the first *) in the place of coupling:



In view of the yield and average (*ca.* octameric) complexity of the polymer it seems likely that dehydrogenation and coupling at the tertiary carbon atoms proceed with only occasional variations caused by two-stage dehydrogenations, which latter must lead, where they occur, to departure from the regular double-row–parallel-plane arrangement formulated in (XV). The coupling, however, seems to be occasionally varied by the inclusion of a *tert.*-butoxy-group in place of *cyclo*hexyl.

Experimental.

(Microanalyses by Dr. W. T. Chambers, Miss E. Farquhar, and Mrs. H. Hughes. Spectrographic observations by Dr. H. P. Koch.)

Di-tert.-*butyl Peroxide.*—The peroxide was prepared by both methods given by Milas and Surgenor (*J. Amer. Chem. Soc.*, 1946, **68**, 205). That prepared from *tert.*-butyl hydroperoxide and *tert.*-butyl hydrogen sulphate had b. p. 109·0—110·0°/761·5 mm., n_D^{16} 1·3905 (Found: C, 65·45; H, 12·65. Calc. for $C_8H_{18}O_2$: C, 65·7; H, 12·4%). Prepared from *tert.*-butanol and hydrogen peroxide, the pure peroxide had b. p. 109·0—110·0°/760 mm., n_D^{20} 1·3882 (Found: C, 65·7; H, 12·3%). Milas and Surgenor (*loc. cit.*) give b. p. 109·0—109·2°/760 mm., n_D^{20} 1·3872; Vaughan and Rust (U.S.P. 2,395,523, Feb. 26th, 1946) give b. p. 108—110°, n_D^{20} 1·3893.

Reaction of Di-tert.-*butyl Peroxide with* cyclo*Hexene.*—The reaction was conducted under various conditions of molar ratio and reaction time, the following being a representative example. The olefin (164 g., 2·0 mols., b. p. 82·50°/744·5 mm., n_D^{20} 1·4463) with di-*tert.*-butyl peroxide (48·7 g., 0·33 mol.) was heated for 48 hours at 140° in Carius tubes sealed in an atmosphere of pure nitrogen. The product (212·0 g.) was a colourless mobile liquid which on fractionation through a 10-in. Vigreux column under nitrogen gave a forerun of b. p. 74—83°/764 mm. (160·6 g.). After removal of the last traces of volatile material by warming the residue at 50° for a short time at the water-pump, there remained a colourless oily product (45·0 g.); this was distilled at oil-pump pressure, giving the fractions: (i) b. p. 68—71°/1 mm. (27·2 g.), n_D^{20} 1·5095, (ii) b. p. 130—140°/1 mm. (9·75 g.), (iii) b. p. 180—192°/1 mm. (3·5 g.), and an undistillable residue (*ca.* 4·2 g.), which set to a glass on cooling.

Reaction products. The forerun, consisting of a mixture of *tert.*-butanol, unchanged *cyclo*hexene, and a trace of acetone, was extracted 6 times with water (6 × 50 g.) whereby 46·0 g. of water-soluble material were obtained. This extract was found to be almost entirely *tert.*-butanol. In one experiment the aqueous extract was distilled, giving an azeotrope of *tert.*-butanol and water, b. p. 80°/763 mm., the butanol component of which (separated and dried by potassium hydroxide, and subsequently distilled over sodium) boiled at 80—82°/765 mm., and was identified by formation of its phenylurethane (m. p. and mixed m. p. with an authentic specimen 135—136°) (Found: C, 68·5; H, 8·3; N, 7·0. Calc. for $C_{11}H_{15}O_2N$: C, 68·4; H, 7·83; N, 7·25%). In a similar experiment the aqueous extract was treated with an excess of saturated 2:4-dinitrophenylhydrazine solution (in 2N-hydrochloric acid). Acetone

* The tendency for this two-stage dehydrogenation to occur in hydroaromatic rings is understandably much greater than is the case for open-chain olefins (cf. Part V). The susceptibility of *tert.*-*cyclo*hexyl groups, such as occur in (XVI), to similar attack, is, doubtless, of a much lower order.

2 : 4-dinitrophenylhydrazone separated (0·24 g. ≡ 0·05 g. of acetone), which on crystallisation from light petroleum (b. p. 100—120°) had m. p. 122—123°, and mixed m. p. with an authentic sample 123—124° (Found : C, 45·7; H, 4·55. Calc. for $C_9H_{10}O_4N_4$: C, 45·4; H, 4·2%). The yield of *tert.*-butanol represented 93·3% of the peroxide taken, the yield of acetone being insignificant (equivalent to <0·1% of peroxide). The recovered *cyclo*hexene (114·5 g.) was dried ($CaCl_2$) and when distilled over sodium (in nitrogen) had b. p. 83·0°/763 mm. Ultra-violet spectrographic analysis of a sample of this olefin showed the almost complete absence of conjugated diene (Found : 0·05—0·1% of *cyclo*hexa-1 : 3-diene), and the complete absence of benzene.

The dimer. Fraction (i), a colourless oily liquid, consisted mainly of the dimeric olefin di*cyclo*hex-2-enyl (Found : C, 88·0; H, 11·2%). On careful fractionation over sodium (in nitrogen) it gave the pure hydrocarbon, b. p. 62—63°/0·5 mm. (68—69°/1·0 mm.), n_D^{18} 1·5092 [Found : C, 88·65; H, 11·23%; I.V., 302·5, 302·2; *M* (micro-Rast), 167·5. Calc. for $C_{12}H_{18}$: C, 88·8, H, 11·2%; I.V. 313·6; *M*, 162]. Quantitative catalytic hydrogenation of the olefin in pure ethanol (Adams's catalyst) gave a value of 1·97 double bonds per molecule (Calc. for $C_{12}H_{18}$: $\overline{2}$). A larger portion (1·5 g.) of the olefin, similarly hydrogenated in ethanol (20 c.c.), absorbed in *ca.* 6 hours 398 c.c. of hydrogen at N.T.P. (Calc. : 415 c.c.), so giving di*cyclo*hexyl, which on distillation over sodium had b. p. 72—73°/*ca.* 1 mm., n_D^{20} 1·4803; the yield was 1·3 g. (86·5%) (Found : C, 86·65; H, 13·4. Calc. for $C_{12}H_{22}$: C, 86·65; H, 13·35%). The olefin (2·0 g.) in chloroform (20·0 c.c.), cooled to −10°, absorbed during 1 hour (with stirring) 3·75 g. of bromine (in 20 c.c. of chloroform). The colourless crystalline product (5·75 g., 96·6%) consisted of a mixture of two, presumably stereoisomeric, di*cyclo*hexenyl tetrabromides, which were separated by repeated fractional crystallisation from chloroform. The more soluble isomer, prismatic plates, m. p. 159—162°, predominated (Found : C, 29·9; H, 3·8; Br, 66·65. Calc. for $C_{12}H_{18}Br_4$: C, 29·9; H, 3·76; Br, 66·75%); the less soluble isomer, large rectangular prisms, was present in only small yields, m. p. 188—190° (Found : C, 29·85; H, 3·75; Br, 66·75%). Both tetrabromides have been reported in the literature, the former as having m. p. 159° (Farmer and Michael, *J.*, 1942, 513), and the latter m. p. 189—190° (Berlande, *Compt. rend.*, 1941, **213**, 484).

For comparison with the dimer, di*cyclo*hex-2-enyl was obtained from 3-bromo*cyclo*hexene and magnesium. The bromide was prepared by the method of Ziegler *et al.* (*Annalen*, 1942, **551**, 80); the *N*-bromosuccinimide (36·6 g.) and *cyclo*hexene (103 c.c.) were refluxed in carbon tetrachloride (150 c.c.) for 30 minutes in the presence of a little benzoyl peroxide as catalyst. The succinimide (20·2 g. Calc. : 20·35 g.) which separated from the cold reaction mixture was filtered off. Removal of the solvent through a column, and distillation of the residue, gave 3-bromo*cyclo*hexene (25·0 g., 75%), b. p. 58—60°/12 mm., $n_D^{18\cdot5}$ 1·5309 (Found : C, 44·75; H, 5·6. Calc. for C_6H_9Br : C, 44·75; H, 5·65%). When this bromide (20·0 g.), dissolved in ether (75 c.c.), was added during 40 minutes to magnesium (2·0 g.), just covered with ether, and the mixture warmed, reaction soon began. When it had subsided, the product was stirred for an hour, then decomposed with ice-cold ammonium chloride solution, and the ethereal layer separated and dried ($CaCl_2$). The extracted di*cyclo*hexenyl when distilled over sodium (in nitrogen) had b. p. 62—63°/0·5 mm., n_D^{19} 1·5093 (yield 9·4 g., 94%) (Found : C, 88·5; H, 11·35. Calc. for $C_{12}H_{18}$: C, 88·8; H, 11·2%). Addition of bromine to this product (2·0 g.), as described above, gave a mixture of tetrabromides (5·95 g., 100%), resolvable into a major isomer of m. p. 160° (Found : C, 29·85; H, 3·85; Br, 66·3%), and a minor one of m. p. 189—190° (Found : C, 29·9; H, 3·8; Br, 66·4%), identical with those previously obtained.

The trimer. Fraction (iii) was a colourless, viscous liquid which on refractionation over sodium (in nitrogen) distilled mainly at 133—134°/1 mm., and had n_D^{20} 1·5330. It represented the " trimeric " olefin *ter*cyclo*hexenyl*, $C_{18}H_{28}$ $\overline{3}$ [Found : C, 88·9; H, 10·85%; I.V., 282, 284, 287; *M* (micro-Rast), 239. $C_{18}H_{28}$ requires C, 89·2; H, 10·8%; I.V., 315; *M*, 242].

Quantitative catalytic hydrogenation of the olefin in glacial acetic acid (Adams's catalyst) showed 2·94 double bonds per molecule. A larger portion (5·0 g.), hydrogenated in a mixture of glacial acetic acid (25 c.c.) and ethyl acetate (15 c.c.) at room temperature and pressure, took up 1435 c.c. of hydrogen at N.T.P. (Calc. : 1390 c.c.). The reaction mixture, from which crystals had already separated, gave, when worked up, a crude saturated hydrocarbon (4·95 g.), from which by distillation (i) a partly crystallising oil, b. p. 147—150°/2 mm. (3·5 g.), and (ii) a colourless crystalline residue (1·45 g.) were obtained. The latter, together with the solid from fraction (i) (0·2 g.), represented the high-melting form of 1 : 4′-ter*cyclo*hexyl, forming colourless, feathery plates, m. p. 162—163° (Found : C, 86·9; H, 13·0. Calc. for $C_{18}H_{32}$: C, 87·0; H, 13·0%), from ethyl acetate (von Braun, Irmisch, and Nelles, *Ber.*, 1933, **66**, 1471, give m. p. 162°; Corson and Ipatieff, *J. Amer. Chem. Soc.*, 1937, **59**, 646, give m. p. 159·5—161°). On redistillation, the colourless liquid from fraction (i) had b. p. 122—128°/1 mm., n_D^{18} 1·5072. It could not be crystallised and consisted, presumably, of a mixture of stereoisomers of 1 : 4′- and 1 : 3′-ter*cyclo*hexyl (Found : C, 87·05; H, 12·6%). For the low-melting form of the 1 : 4′-isomer, Corson and Ipatieff (*loc. cit.*) reported m. p. 54—56°, and later (*ibid.*, 1938, **60**, 747) for the two forms of the 1 : 3′-isomer the m. p.s 62·5—63·5° and 57—59°.

Dehydrogenation of the trimeric olefin (2·0 g.) was effected by heating it with powdered selenium (6·0 g.), in nitrogen, for 40 hours at 320° (metal-bath). Evolution of hydrogen selenide began almost immediately. The product, which solidified on cooling, was extracted with boiling benzene. The extract gave a solid (1·8 g.), which by sublimation over molten sodium at 0·05 mm. (bath-temp. 200—250°) gave a colourless crystalline mass (1·53 g.) melting over the range *ca.* 50° to *ca.* 175°. Crystallisation of this product from benzene gave *p*-terphenyl (0·4 g.) as lustrous plates, m. p. 211—212° (lit. 213°) (Found : C, 93·35; H, 6·15. Calc. for $C_{18}H_{14}$: C, 93·9; H, 6·1%). The benzene mother-liquor was evaporated to dryness, and the resulting solid (0·99 g.) repeatedly crystallised, whereby the following fractions were obtained : (i) a mixture of *p*- and *m*-terphenyl (0·6 g.); (ii) *m*-terphenyl as colourless needles, m. p. 82° (softening)—84° (0·15 g.) (Found : C, 94·0; H, 6·1%), and (iii) a less pure *m*-terphenyl, m. p. 82—83° (0·13 g.). (The highest recorded m. p. for this substance is 87°.)

Addition of bromine (1·5 c.c. in 20 c.c. of chloroform) to the olefin (2·0 g.) in chloroform (20 c.c.) at 0° yielded a difficultly separable mixture of isomeric *ter*cyclo*hexenyl hexabromides* (5·4 g.). Fractional crystallisation of this mixture from chloroform gave the following fractions: (*a*) a very insoluble, colourless, crystalline powder (0·1 g.), m. p. 285—287° (sublimation) (Found: C, 29·95; H, 3·7; Br, 66·55. $C_{18}H_{24}Br_6$ requires C, 29·95; H, 3·62; Br, 66·4%); (*b*) a colourless microcrystalline powder, m. p. 249—250° (*ca.* 50 mg.); (*c*) the major product, colourless micro-crystals, m. p. 217—219° (Found: C, 29·95; H, 3·7; Br, 67·0%).

The tetramer. Redistillation of fraction (iii) over sodium (in nitrogen) gave a colourless, extremely viscous liquid, b. p. 180—193°/1 mm., n_D^{20} 1·5478, having the composition of *quater*cyclo*hexenyl* [Found: C, 89·05; H, 10·7%; I.V. 282, 284; *M* (micro-Rast), 313. $C_{24}H_{34}[\bar{4}]$ requires C, 89·35; H, 10·65%; I.V., 313·5; *M*, 322]. Although molecularly homogeneous, it doubtless contained many structural isomers. This tetrameric mixture (29·62 mg.), dissolved in glacial acetic acid (5·0 c.c.), absorbed 8·65 c.c. of hydrogen at 13° and 753 mm. (*i.e.*, 3·98 mols. per molecule) in presence of Adams's catalyst (10 mg.).

Ultra-violet spectrographic analysis of the polymeric products. The di- and ter-*cyclo*hexenyls isolated showed no selective absorption consistent with the presence of conjugated dienes. Quater*cyclo*hexenyl from the 1 : 6 run (Table I), in *cyclo*hexane–ethanol (9 : 1) as solvent, showed selective absorption near $\lambda_{max.}$ 2450 A., $E^{1\%}_{1\,cm.}$ ~45, and also at ~$\lambda_{max.}$ 2830 A., $E^{1\%}_{1\,cm.}$ ~50. The same olefin from the 1 : 4 run (Product A, Table II), in *cyclo*hexane–ethanol (1 : 1) as solvent, showed selective absorption at $\lambda_{max.}$ 2430 A., $E^{1\%}_{1\,cm.}$ 50, and at $\lambda_{max.}$ 2860 A., $E^{1\%}_{1\,cm.}$ 65. The polymeric mixture obtained as the undistillable residue from the 1 : 4 run (Product B, Table II), in *cyclo*hexane–ethanol (1 : 1) showed selective absorption at $\lambda_{max.}$ 2430 A., $E^{1\%}_{1\,cm.}$ 140, and at $\lambda_{max.}$ 2860 A., $E^{1\%}_{1\,cm.}$ 45. The polymeric mixture in the 1 : 2 run (Product C, Table II) gave similar bands at $\lambda_{max.}$ 2430 A., $E^{1\%}_{1\,cm.}$ 180, and at $\lambda_{max.}$ 2860 A., $E^{1\%}_{1\,cm.}$ 90.

*Reaction of Di-*tert.*-Butyl Peroxide with Dicyclohex-2-enyl.*—The olefin (16·2 g.; b. p. 68—70°/1 mm.) and di-*tert.*-butyl peroxide (7·3 g.) were heated at 140° for 48 hours in an evacuated sealed tube. The product (23·0 g.) gave on distillation the following fractions: (i) *tert.*-butanol, b. p. 80—82·5°/751 mm. (6·8 g., equivalent to 92% of the peroxide taken); (ii) unchanged olefin, b. p. 64—67°/*ca.* 1 mm., n_D^{20} 1·5090 (5·8 g. or 35·8% of the olefin taken) (Found: C, 88·45; H, 11·4%); (iii) an oil of b. p. 180—190°/1 mm., n_D^{20} 1·5468 (3·0 g.); and (iv) the residue in the still (6·6 g.), which set on cooling to a bright orange resin.

Fraction (iii) resembled in all respects the quater*cyclo*hexenyl previously obtained from *cyclo*hexene [Found: C, 89·35; H, 10·8%; I.V., 289, 292; unsaturation value (catalytic hydrogenation), $\bar{f}_{3\cdot64}$. Calc. for $C_{24}H_{34}$: C, 89·36; H, 10·64%; I.V., 315·5; $[\bar{4}]$.

Fraction (iv) consisted mainly of a cyclo*hexene polymer* mixture having, on average, " octameric " complexity [Found: I.V., 307·3, 307·5; *M* (micro-Rast), 666. $C_{48}H_{66}[\bar{8}]$ requires I.V., 316; *M*, 643].

*Reaction of Di-*tert.*-butyl Peroxide with Hept-1-ene.*—The olefin was prepared by the reaction of allyl bromide with *n*-butylmagnesium bromide (cf. Wilkinson, *J.*, 1931, 3057) and fractionated (in nitrogen) over sodium through a 3-ft. Widmer column. It had b. p. 92·0—93·2°/746 mm., n_D^{20} 1·3999 (Found: C, 85·6; H, 14·8. Calc. for C_7H_{14}: C, 85·6; H, 14·4%).

A mixture of the olefin (85·0 g.) and di-*tert.*-butyl peroxide (31·7 g.) was heated at 140° for 24 hours in nitrogen-filled Carius tubes. The product (116·0 g.), a light yellow oil, gave on fractionation the fractions: (i) b. p. 75—86° (32·5 g.), (ii) b. p. 84—100°/1 mm., n_D^{20} 1·4410 (9·1 g.) (Found: C, 84·6; H, 14·35%), and (iii) a residue (64·5 g.).

Examination of the fractions. Aqueous extraction of the forerun (i) gave *tert.*-butanol (27·1 g., *i.e.*, 85·5% of the peroxide taken) and recovered olefin (5·4 g.), the latter of which, after being dried ($CaCl_2$) and distilled over sodium, had b. p. 94·0—96·5°/766 mm., n_D^{20} 1·4000.

A portion (5·0 g.) of fraction (ii), on refractionation over sodium through a 6-in. column, gave the three sub-fractions: (iiA), b. p. 58—70°/0·1 mm., n_D^{24} 1·4420 (1·1 g.) [Found: C, 85·2; H, 14·35%; *M* (in benzene), 196. Calc. for $C_{14}H_{28}$: C, 85·6; H, 14·35%; *M*, 196. Calc. for $C_{14}H_{26}$: C, 86·5; H, 13·5%; *M*, 194]; (iiB), b. p. 70—76°/0·1 mm., n_D^{24} 1·4440 (1·85 g.) [Found: C, 85·8; H, 14·45; *M* (in benzene), 207, 208, 209]; (iiC), b. p. 76—78°/0·1 mm., n_D^{24} 1·4430 (1·65 g.) [Found: C, 85·1; H, 14·6%; *M* (in benzene), 211]. Quantitative catalytic hydrogenations of these sub-fractions in glacial acetic acid, over Adams's catalyst, gave the following hydrogen uptake values: (iiA), 98·6 c.c. (N.T.P.)/g., 97·85 c.c./g.; (iiB), 83·8 c.c./g.; (iiC), 93·7 c.c./g. (Calc. for $C_{14}H_{28}[\bar{1}]$: 114·3 c.c./g. Calc. for $C_{14}H_{26}[\bar{3}]$: 231·0 c.c./g.).

The original residue, fraction (iii), was a mixture of polymeric hydrocarbons of unsaturation value considerably lower than that of the parent olefin [Found: C, 85·7; H, 14·0%; *M* (in benzene), 590]; n_D^{20} 1·4737. It absorbed 34·7 c.c./g. (N.T.P.) (Adams's catalyst) (Calc. for $C_{42}H_{84}[\bar{1}]$: C, 85·6; H, 14·4%; *M*, 588; Hydrogen uptake, 38·1 c.c./g.).

Infra-red spectrographic analysis of hept-1-ene and the derived olefins. The various samples of the heptene products were examined as the pure liquids in rock-salt absorption cells of path length 0·1 mm. on a Hilger double-beam research instrument run on a single-beam photographic recording. The synthetic hept-1-ene employed had very strong bands at 909 and 990 cm.$^{-1}$. Selective absorption of other characteristic frequencies was absent. The recovered hept-1-ene contained, in addition to the 909 and 990 cm.$^{-1}$ bands, an extremely weak band at 965 cm.$^{-1}$. The dimer sub-fractions (iiA), (iiB), and (iiC) had spectra very similar to one another. In addition to strong absorption at 910 and 990 cm.$^{-1}$, they displayed a strong band at 965 cm.$^{-1}$ and other bands at 1082 and 1198 cm.$^{-1}$ and a weak band at 887 cm.$^{-1}$. In the (residual) polymer mixture (iii), by far the strongest absorption occurred at 965 cm.$^{-1}$.

*Reaction of Di-*tert.*-butyl Peroxide with Alkylbenzenes.—Products from toluene.* A mixture of the peroxide (18·25 g., 1 mol.) and toluene (46·0 g., 4 mols.; b. p. 100·0—100·2°/761 mm., $n_D^{19\cdot2}$ 1·4974) was heated at 140° for 24 hours in a Carius tube sealed under nitrogen. When the tube was opened a considerable amount of gas was evolved. The liquid product (*ca.* 64 g.) gave on distillation the following three fractions: (i) b. p. 79—110° (31·5 g.), containing (*a*) unchanged toluene, (*b*) peroxide, (*c*) *tert.*-butanol (12·3 g.) (phenylurethane, m. p. 135·5—136°. Found: C, 68·3; H, 7·65; N, 7·4. Calc. for $C_{11}H_{15}O_2N$: C, 68·4; H, 7·8; N, 7·25%), and (*d*) acetone (1·1 g.) (2 : 4-dinitrophenylhydrazone, m. p. 124—125°. Found: C, 45·45; H, 4·35. Calc. for $C_9H_{10}O_4N_4$: C, 45·4; H, 4·25%); (ii) b. p. 110° (15·15 g.), n_D^{20} 1·4927, consisting mainly of unchanged toluene; (iii) b. p. 84—85°/0·1 mm. (0·4 g.); (iv) dibenzyl, b. p. 85—86°/0·1 mm., m. p. 51·0—51·5° (4·2 g.) (Found: C, 92·25; H, 7·75. Calc. for $C_{14}H_{14}$: C, 92·25; H, 7·75%); (v) b. p. 86—138°/0·1 mm. (0·4 g.); (vi) a saturated oil, b. p. 138—144°/0·1 mm., $n_D^{19\cdot2}$ 1·5872 (2·3 g.), consisting mainly of but slightly impure 1 : 2 : 3-*triphenylpropane* (Found: C, 92·05; H, 7·6. $C_{21}H_{20}$ requires C, 92·6; H, 7·4%); and (vii) a slightly oxygenated undistillable residue (7·15 g.), which set to a clear light yellow glass (Found: C, 90·75; H, 7·65%).

Products from Ethylbenzene.—The peroxide (36·5 g., 1 mol.) and ethylbenzene (106 g., 4 mols.; b. p. 135°/755 mm., n_D^{20} 1·4959) were heated on an oil-bath under an efficient reflux at 140° for 24 hours, a slow stream of purified nitrogen being passed through the apparatus. The product (142·0 g.) gave on distillation a liquid, b. p. 83—136°/760 mm. (125·0 g.), shown by aqueous extraction to contain *tert.*-butanol (*ca.* 12·7 g.) and a residue. Removal of the last traces of ethylbenzene from the latter by heating it on a water-bath under slightly diminished pressure gave a partly crystallising product (16·3 g.), from which crystals of *meso*-2 : 3-diphenylbutane (7·5 g.), m. p. 125—126° were isolated (Found: C, 91·5; H, 8·75. Calc. for $C_{16}H_{18}$: C, 91·35; H, 8·65%): Conant and Blatt (*J. Amer. Chem. Soc.*, 1928, **50**, 551) record m. p. 124—125°, and Ott (*Ber.*, 1928, **61**, 2139) records m. p. 126—127°. The oily liquid (8·8 g.) accompanying the crystals gave on distillation a fraction, b. p. 85—86°/1 mm. (6·3 g.), from which more solid of m. p. 126° (0·9 g.) was separable, leaving a colourless oily liquid (5·4 g.) consisting mainly of racemic 2 : 3-diphenylbutane. On redistillation of this liquid over sodium it had b. p. 136°/9 mm., n_D^{20} 1·5537 (Found: C, 91·25; H, 8·8%). Kharasch, McBay, and Urry (*J. Org. Chem.*, 1945, **10**, 401) give b. p. 106°/2 mm., n_D^{20} 1·5517. Isomerisation of the racemic to the *meso*-form of diphenylbutane (m. p. 126°) was effected by heating the former in an evacuated sealed tube at 250° for 17 hours in the presence of a small quantity of iodine (<1 mg. per g. of hydrocarbon); the yield was 42%. The residue (2·5 g.) in the still was a colo[u]rless viscous liquid, consisting of higher polymeric hydrocarbons.

Products from iso*Propylbenzene.*—A mixture of the peroxide (12·2 g.; 1 mol.) and *iso*propylbenzene (20·0 g., 2 mols.; b. p. 148·0—148·5°/725 mm., n_D^{20} 1·4910) was heated under an efficient reflux condenser on an oil-bath at 140° for 46 hours, purified nitrogen being passed through the apparatus. The product, on fractionation, gave: (i) mainly *tert.*-butanol (5·1 g.), b. p. 82—83° (phenylurethane, m. p. 136°); (ii) unchanged peroxide, b. p. 110—114° (6·2 g.); (iii) unchanged hydrocarbon, b. p. 150—152° (11·25 g.), and (iv) still residue, solid 2 : 3-dimethyl-2 : 3-diphenylbutane (8·45 g.), which crystallised from absolute ethanol in long colourless needles, m. p. 118—119° (Found: C, 90·6; H, 9·4. Calc. for $C_{18}H_{22}$: C, 90·7; H, 9·3%). Klages (*Ber.*, 1902, **35**, 2638) gives m. p. 119—120°, and Kharasch *et al.* (*loc. cit.*) m. p. 115°.

In a second experiment the peroxide (12·2 g.; 1 mol.) and *iso*propylbenzene (40·0 g., 4 mols.), after being heated in nitrogen-filled Carius tubes at 140° for 24 hours, gave: (i) *tert.*-butanol (9·8 g., equiv. to 79·5% of the peroxide taken), (ii) acetone (0·5 g.) estimated and identified as its 2 : 4-dinitrophenylhydrazone (2·15 g.), (iii) a mixture of unchanged peroxide and hydrocarbon (23·3 g.), and (iv) dimethyldiphenylbutane, m. p. 118—119·5° (17·1 g.; 85·5%, based on the peroxide consumed).

*Reaction of Di-*tert.*-butyl Peroxide with* cyclo*Hexane.*—The peroxide (24·3 g., 1 mol.) and spectroscopically pure *cyclo*hexane (84·0 g., 6 mols.; n_D^{20} 1·4262) were heated together in Carius tubes at 140° for 24 hours. The product (107·9 g.), a light yellow liquid, gave on distillation a forerun, b. p. 70—91°/766 mm. (92·5 g.), shown by aqueous extraction and treatment of the aqueous extract with 2 : 4-dinitrophenylhydrazine solution (2N-hydrochloric acid) to contain *tert.*-butanol (22·8 g., equiv. to 92·45% of peroxide taken), acetone (0·085 g.), and unchanged *cyclo*hexane (*ca.* 69 g., n_D^{20} 1·4261).

The polymeric product (13·6 g., equiv. to 16·2% of the hydrocarbon taken) was a viscous yellow liquid which on fractionation gave: (i) b. p. <100°/11 mm., n_D^{20} 1·4711 (0·34 g.); (ii) b. p. 100·0—102·3°/11 mm., n_D^{20} 1·4784 (3·08 g.); (iii) b. p. <124°/0·1 mm., n_D^{20} 1·4825 (0·57 g.); (iv) b. p. 124—134°/0·1 mm., n_D^{20} 1·5035 (0·57 g.); and (v) an orange polymeric residue (7·1 g.) which on cooling set to a brittle solid glass. Fraction (ii), consisting mainly of di*cyclo*hexyl, gave on refractionation over sodium a small forerun, b. p. <99·5°/10 mm., n_D^{20} 1·4792, together with a main fraction, b. p. 99·5—100·0°/10 mm., n_D^{20} 1·4801 (Found: C, 86·8; H, 13·4. Calc. for $C_{12}H_{22}$: C, 86·65; H, 13·35%). Fraction (iv) was mainly ter*cyclo*hexyl, but contained a small amount of oxygenated material [Found: C, 86·3; H, 12·6%; *M* (in benzene), 242. Calc. for $C_{18}H_{32}$: C, 87·0; H, 13·0%; *M*, 248]. Fraction (v) was mainly a mixture of polymeric hydrocarbons but also contained a small amount of oxygen [Found: C, 87·0; H, 11·5%; *M* (in benzene), 630]. An ultra-violet spectrographic examination of this polymer indicated the presence of unsaturation and, in particular, showed selective absorption near $\lambda_{max.}$ 2550 A., which is attributed to the presence of not more than 5% of conjugated *cyclo*hexadiene groupings.

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[*Received, July 26th*, 1950.]

30. *Radical Mechanisms in Saturated and Olefinic Systems. Part II. Disubstitutive Carbon–Carbon Cross-linking by* tert.*-Alkoxy-radicals in Isoprenic Olefins and Rubber.*

By E. H. Farmer and C. G. Moore.

The high degree of dehydrogenation effected by *tert.*-butoxy-radicals at the α-methylenic groups of olefins enables these radicals to be used for the carbon-to-carbon cross-linking of unsaturated carbon chains, and especially of the polyisoprenic chains of natural rubber. Such cross-linking amounts to a vulcanisation process in which the connecting links between chain molecules are just C–C bonds, which may be expected to have appropriate attributes.

An examination has first been made of the cross-linking produced by *tert.*-butoxy-radicals (from di-*tert.*-butyl peroxide) at 140° between the short isoprenic chains in 1-methyl*cyclo*hexene, 4-methylhept-3-ene, 2 : 6-dimethylocta-2 : 6-diene, and digeranyl. Cross-linking proceeds efficiently in each case, and the points of union in these isoprene units which become directly joined are not confined to *original* α-methylenic carbon atoms. Where the reagent radicals are in considerable deficit (*e.g.*, one per two or three of the isoprene units present) those olefin molecules which are attacked become linked together mostly by single unions to form aggregates containing two, three, or four molecules; but in the tetraisoprenic olefins the extent to which more than one union is formed between some of the directly linked molecules becomes appreciable.

In natural rubber, cross-linking occurs smoothly and to nearly the full extent corresponding to the (in practice restricted) proportion of peroxidic reagent employed. Good vulcanisates can be so obtained in which the tensile strength is found to increase towards a maximum and then to decline rapidly as the degree of cross-linking steadily increases. Thus to obtain vulcanisates of the optimum physical characteristics the degree of cross-linking must be suitably chosen. The rôle of the peroxidic reagent is almost entirely non-additive and non-degradative.

The efficiency of *tert.*-butoxy-radicals in dehydrogenating olefinic and paraffinic hydrocarbons, thereby permitting the coupling of the resulting radicals, has been demonstrated in Part I (preceding paper). The process provides a ready means for cross-linking carbon chains by carbon-to-carbon bonds; moreover, by repetition of the process in long chains an increasing degree of cross-linking can be obtained. It is of considerable practical interest to observe the effect on the physical properties of long-chain hydrocarbons (and especially of polyisoprenic and polybutadienic rubbers) of increasing gradually the proportion of carbon–carbon cross-links per molecule for ultimate comparison with corresponding effects in the sulphur-bridge cross-linking of the same chains, which (so far as is known) is mainly of substitutive–additive type, the bridges containing 1—6 sulphur atoms. The present account deals principally with the cross-linking of natural rubber molecules by radicals, but briefly reports also a series of preliminary experiments carried out with short-chain olefins (" model " rubber molecules) containing 1—4 isoprene units. For comparison with rubber, it was desirable to have all the isoprene units of the model molecules of the unmodified " rubber-type," $-\overset{\alpha}{C}H_2-\overset{\beta}{C}Me=\overset{\gamma}{C}H-\overset{\delta}{C}H_2-$, which, because of the primary character of the methylic C–H bonds, would not be liable to undergo any very appreciable degree of attack at other than the two secondary α-methylene groups. But obviously this was only partly feasible, since all the terminal isoprene units of relatively short-chain polyisoprenes necessarily have their outermost α-methylene groups embodied in (primary) methyl groups, so making the comparison with rubber not quite exact in respect of the distribution of radical attack. It is particularly to be noted that the two isoprene units of the most readily available model molecule, dihydromyrcene (or, better, its synthetic counterpart, 2 : 6-dimethylocta-2 : 6-diene, which does not contain the occasional vinylic isoprene units, $CH_2{:}CMe{\cdot}CH_2{\cdot}CH_3$, to which naturally occurring terpenic chains are liable), each contain only one secondary α-methylene group, so that attack on the molecule by radicals, provided that not more than one radical per unit is employed, is likely to be almost wholly confined to the mid-chain pair of methylene groups. In order to ensure that every *tert.*-butoxy-radical may have a good

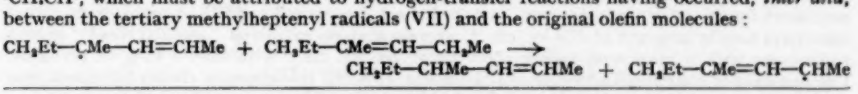
chance of encountering an unattacked isoprene unit, the initial concentration of the former has been restricted to an average of one per two isoprene units in the case of monoisoprenes, and to one per three units in that of di- and tetra-isoprenes. Hence, the maximum average degree of cross-linking which can ensue falls far short of one cross-link emanating from every unit of every chain. The mono-olefins selected for examination are two disubstituted isoprenes, $R{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CH_2R'$, in the first of which the groups R and R′ are polarly equal (since they consist of the same system $\cdot CH_2{\cdot}CH_2\cdot$), and in the second are polarly unequal, so that the distribution of negative activation * within the isoprenic system may be considered normal in the first and somewhat unbalanced in favour of C_δ in the second.

The Cross-linking of 1-*Methyl*cyclo*hexene and of* 4-*Methylhept-3-ene*.—Dehydrogenation of the two secondary α-methylenic groups in 1-methyl*cyclo*hexene can give only the radical forms (I—III), since the amount of attack at the methyl group (as experience in such cases confirms)

(I.) (II.) (III.) (IV.)

is likely to be negligible. Of these three, two are resonance forms of the mesomeric radical (IV). By the coupling of the three forms in pairs a maximum of six structurally different dimers becomes possible, and by the further coupling of the original and the new radical forms still larger numbers of isomeric trimers and isomeric higher polymers are likely to arise. In practice, fractions consisting of dimers ($C_{14}H_{22}$, $\overline{2}$), trimers ($C_{21}H_{33}$, $\overline{3}$), tetramers ($C_{28}H_{42}$, $\overline{4}$), and higher polymers † were readily separated in relative proportions of about 5 : 2 : 1 : 2. The individual isomers constituting the dimer could not be separated by distillation, or by fractionation of their tetrahydrides or tetrabromides; and, in view of the rather complicated character of the degradative scission products to be expected, no detailed analysis of structural forms was attempted.

The polar inequality between the ethyl and methyl groups in 4-methylhept-3-ene may be expected to enhance slightly the negative activation at C_δ (V) relative to that in an ordinary rubber unit, in which the flanking alkenylmethyl groups, RR′, although different in size and detail, may be considered polarly equal. This should cause a somewhat increased degree of substitutivity at C_δ, and of course at the corresponding resonance position C_β. By treatment of the olefin with the peroxide, the usual mixture of dimers and higher polymers was obtained. The dimer fraction ($C_{16}H_{30}$, $\overline{2}$) was composed of a mixture of hexadecadienes, which was shown by infra-red spectrographic examination to contain olefinic groupings of the type, RR′C:CHR″, characterising the original olefin and its derived radicals (VI and VIII),‡ as well as of a new type, RCH:CHR, doubtless resulting from incorporation in the dimers of the resonance form (VII). The proportion of the new grouping, as deduced from the relevant extinction coefficient,



was computed to be *ca.* 15%, which value is at least equal to that found for comparable (resonance-sited) C_β-substitution in 2-methylbut-2-ene (Part III). It was of interest that the recovered monomeric olefin gave evidence of containing traces of unsaturation of the type $\cdot CH{:}CH\cdot$, which must be attributed to hydrogen-transfer reactions having occurred, *inter alia*, between the tertiary methylheptenyl radicals (VII) and the original olefin molecules:

$$CH_2Et{-}CMe{-}CH{=}CHMe + CH_2Et{-}CMe{=}CH{-}CH_2Me \longrightarrow CH_2Et{-}CHMe{-}CH{=}CHMe + CH_2Et{-}CMe{=}CH{-}CHMe$$

* The method of degradative analysis adopted elsewhere (Parts V and VII) is unsuitable for examining in detail the effect of altering the negativisation balance in favour of C_α or C_δ by using in turn different electron-donating substituents R and R′. Doubtless, study of the rates of substitutive (radical) reaction in the differently substituted olefinic chains, as in maleinisation, oxidation, and sulphuration, would be more effective.

† Actually all dehydropolymers (see preceding paper).

‡ A proportion of the dimer molecules contained, as expected, groupings of the type $CH_2{:}CRR'$, since the olefin sample employed was prepared by dehydration of $CHMePr_2{\cdot}OH$, and so contained a little of the difficulty removable vinylic isomer, $CH_2{:}CPr_2$.

The Cross-linking of 2 : 6-*Dimethylocta*-2 : 6-*diene and of Digeranyl.*—The dimers, trimers, etc., obtained from the first (di-isoprenic) olefin could not be satisfactorily separated by distillation owing to their high boiling point: hence, the presence of more than one cross-link connecting a pair of molecules could not easily be ascertained. The polymer mixture, when freed from unchanged monomer, proved to contain olefinic groupings of the original type, $RR'C{:}CHR''$, as well as quite an appreciable proportion of the type $R{\cdot}CH{:}CHR'$, and even some of the type $RR'C{:}CH_2$. This result was to be expected, but the additional observation that the polymer mixture showed only 82% of the original olefinic unsaturation had not been foreseen. The loss of unsaturation could only have been due to partial cyclisation, and the appearance of the latter in this example must apparently be deemed to result from the carbon chain now being of suitable length, unsaturation-pattern, and negative activation at one end of the double bond for intramolecular radical–double bond additions to succeed; *e.g.*,

$$\dot{C}Me_2{-}CH{=}CH{-}CH_2{-}CMe{=}CH{\cdot}CH_3 \longrightarrow CMe_2{-}CH{=}CH{-}CH_2{-}\dot{C}Me{-}CHMe.$$

The second (tetra-isoprenic) olefin $H[CH_2{\cdot}CMe{:}CH{\cdot}CH_2]_2{\cdot}[CH_2{\cdot}CH{:}CMe{\cdot}CH_2]_2H$ contained, in the main, two ordinary isoprenic units (these being arranged in tail-to-tail fashion);* and two possessing only one secondary α-methylene group each. In spite of the above-mentioned deficiency of reagent employed (one *tert.*-butoxy-radical per three units), one-fifth of the olefin molecules taken remained unlinked, so that (on average) only about 0·8 cross-link per digeranyl molecule could have been formed. In the process, just over three-quarters of the digeranyl molecules had become converted into tetrameric aggregates by cross-linking, so that within these tetramer molecules most of the pairs of digeranyl chains were joined (on average) only by one cross-link, although occasional pairs (*ca.* 2 per 5 tetramers) were joined by two. Some reduction in the original degree of unsaturation occurred in these polymers also, and this again must be attributed to the occurrence of a minor degree of additive (radical to double bond) cyclisation.

The Cross-linking of Rubber.—In the case of rubber, with its average of *ca.* 5000 isoprene units per molecule, observations of cross-linking were made at 100° and at 140° with raw (" smooth smoked sheet ") and acetone-extracted samples, varying proportions of di-*tert.*-butyl peroxide being used as reagent. The specimens became progressively insoluble in benzene and other solvents and showed mechanical properties and swelling characteristics indicating the progressive occurrence of vulcanisation. Determination of the " equilibrium swelling constant " (Q_m) † of the vulcanised specimens, immediately after their preparation, permitted an estimate to be made of the average molecular weight between junction points (M_c) in the cross-linked chains, the latter value being inversely proportional to the number of new cross-links formed (Gee, *J. Polymer Sci.*, 1947, **2**, 451).

The numerical results obtained for the physical characteristics of the cross-linked samples are given in Tables I and II. These demonstrate very clearly that di-*tert.*-butyl peroxide is highly effective in producing good rubber vulcanisates, and the physical nature of the samples indicates that uniform vulcanisation has been effected. The values of Q_m and M_c steadily decrease with increasing peroxide concentration, thereby indicating a progressive increase in the degree of cross-linking.

The figure shows the effect of peroxide concentration on the tensile strengths of the samples The two curves show the characteristic features of well-defined maxima, the tensile strengths increasing with increasing amounts of peroxide up to a certain critical peroxide concentration, beyond which they fall very sharply.‡ The effect of the removal of non-rubber constituents (resin acids, antioxidants, *etc.*) from the rubber by acetone-extraction is to increase the maximum attainable tensile strength and also to reduce the peroxide concentration required to produce this maximum figure. For instance, raw " smoked sheet " requires *ca.* 2·9% of peroxide to give a maximum tensile strength of 178 kg. cm.$^{-2}$, whereas acetone-extracted " smoked sheet " gives a vulcanisate with a maximum tensile strength of 206 kg. cm.$^{-2}$ with only 1·45% of peroxide. The non-rubber constituents presumably compete with the polyisoprene chains for interaction with the peroxide, and so diminish the efficiency of the peroxide as a cross-linking agent.

As the peroxide concentration increases beyond a certain optimum value, the desirable properties of the vulcanisates (good tensile strength and elasticity) deteriorate; and with

* The digeranyl employed contained a minor proportion of *iso*digeranyl in which one of the isoprenic units is modified (private communication).

† Q_m is defined as the volume of solvent (benzene) imbibed at equilibrium swelling by unit volume of rubber.

‡ The same phenomenon is observed with rubber-sulphur vulcanisates (Gee, *loc. cit.*).

TABLE I.

Reaction of raw rubber with di-tert.-butyl peroxide (6 hours at 140°).

Peroxide (g./100 g. of rubber).	Q_m.	10^3M_c.	T.s. (kg. cm.$^{-2}$).	E.b. (%).	Modulus (kg. cm.$^{-2}$). 100%.	300%.	500%.	700%.
0	—	—	54	925	3·1	3·6	4·9	18
1·45	4·4	7·5	141	645	5·4	13	29	—
2·1	3·9	6·1	145	580	7·4	18	60	—
2·5	3·7	5·7	162	570	6·2	20	82	—
2·9	3·4	4·7	178	555	11	22	93	—
3·4	2·6	3·1	123	470	8·2	25	—	—
5·4	2·2	2·3	29·5	250	13	—	—	—
7·65	2·1	2·2	16	85	—	—	—	—
10·1	1·3	1·0	12	40	—	—	—	—
15·7	1·0	0·85	12	20	—	—	—	—

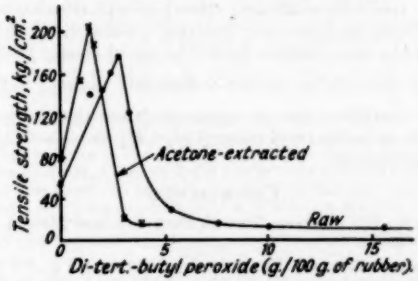
TABLE II.

Reaction of acetone-extracted rubber with di-tert.-butyl peroxide.

Peroxide (g./100 g. of rubber).	Reaction conditions: hrs.	temp.	Q_m.	10^3M_c.	T.s. (kg. cm.$^{-2}$).	E.b. (%).	Modulus (kg. cm.$^{-2}$). 100%.	300%.	500%.	700%.
0	—	—	—	—	80	900	3·3	5·7	11	34
1·0	6	140°	4·3	7·4	155	705	7·3	14	32	154
1·45			4·1	6·8	206	660	6·5	16	56	—
1·7			4·1	6·8	190	625	6·6	17	64	—
3·1			2·6	3·0	22	210	12	—	—	—
3·95			2·1	2·2	16	100	16	—	—	—
51·5			0·74	0·44	—	—	—	—	—	—
2·4	24	99·5° ± 0·5°	8·7	—	109	905	—	6·7	14	43
3·0			8·0	—	>95	835	—	6·9	14	46
3·5			7·2	—	>116	875	—	6·6	15	49
4·5			6·6	—	148	890	—	6·7	16	55
5·0			6·2	—	>137	865	—	6·9	16	55
3·0	72	99·5° ± 0·5°	5·5	—	184	815	—	11	30	104
3·55			6·0	—	172	820	—	9·4	26	90

peroxide concentrations of *ca.* 5—16% the samples show a substantial loss of rubber-like properties, displaying brittleness, low tensile strength, and negligible elasticity. The results thus demonstrate that cross-linking of rubber chains must be restricted within very narrow limits to give useful products.

Cross-linking of rubber at 140° (6 hours).



The increase in oxygen content of the peroxide-vulcanised samples was only very small (0·34—0·355%), as based on direct oxygen determination (Chambers, Rubber Technology Conf., London, 1948, Preprint No. 16), for much of the peroxide was converted into a mixture of *tert.*-butanol and acetone: in one rather extreme case investigated [peroxide equal to 48·2% (w/w) of the rubber; 6 hours' heating], these represented (respectively) 41·1% and 36·6% of the peroxide taken. Thus the major, and probably the sole olefinic reaction in the peroxide-vulcanisation of

rubber is still dehydro-cross-linking, producing ultimately a three-dimensional net-structure in which all the cross-links are C–C bonds. Decomposition of some of the *tert.*-butoxy-radicals to yield acetone will simultaneously give methyl radicals ($Me_3C{-}O\cdot \longrightarrow Me_2CO + Me\cdot$), a part of which may dimerise without any cross-linking effect, and the remainder participate in the dehydrogenation which precedes cross-linking ($RH + Me\cdot \longrightarrow MeH + R\cdot$; $R\cdot + R\cdot \longrightarrow R{-}R$, where R is an isoprene unit of a rubber chain). The likelihood, however, of a portion of the dehydrogenating capacity being lost through acetone-formation will become less as the peroxide concentration decreases, and is probably insignificant up to the optimum concentration value of the rubber. The scanty incorporation of *tert.*-butoxy-radicals in the rubber, as indicated by the low oxygen content, is in sharp contrast to the heavy incorporation of (the more electrophilic) benzoyloxy-radicals in the corresponding treatment of rubber with dibenzoyl peroxide (van Rossem *et al.*, *Kautschuk*, 1931, **7**, 202, 220; Farmer and Michael, *J.*, 1942, 513); moreover, the contrast corresponds to a notable difference between the two peroxidic reagents, since the extensive and wasteful formation of ester characterising the benzoyl compound has no counterpart (ether formation) in the case of the alkyl compound.

TABLE III.

Reaction of acetone-extracted rubber with diethyl peroxide.

Peroxide (g./100 g. of rubber).	Reaction conditions: hrs.	temp.	Q_m.	T.s. (kg. cm.$^{-2}$).	E.b. (%).	Modulus (kg. cm.$^{-2}$). 300%.	500%.	700%.
1·2	6	140° ± 0·5°	7·0	> 90	830	6·6	13	43
1·5			6·7	>102	830	7·6	14	53
2·8			5·4	>116	790	8·9	20	69
3·7			5·1	161	825	9·8	19	82
0·94	6	99·5° ± 0·5°	*	36	835	5·7	7·6	21
1·9			*	34	825	5·0	7·0	18
2·7			*	33	780	4·9	7·8	23
3·6			*	41	825	4·0	8·0	23

* Q_m values too high to be obtained accurately.

It was attractive to investigate whether by use of a rather more energetic alkoxy-radical than the *tert.*-butyl compound superior peroxide-vulcanisates could be obtained from natural rubber by operating at temperatures well below the usual reaction temperature of 140°. To this end the ethoxy-radical, derived by thermal decomposition of diethyl peroxide, was employed. The relevant physical properties of the cross-linked rubbers obtained at 140° and at *ca.* 100° are given in Table III. These, however, reveal that no advantage accrues by using the more reactive but less easily manipulated peroxide. Whether or not the cross-linked products obtained by use of the ethoxy-radical resemble those obtained by use of the *tert.*-butoxy-radical in being almost entirely free from combined ethoxy-groups remains to be investigated. It is possible that ethoxy-radicals are sufficiently energetic (unstabilised) to unite reasonably rapidly with olefinic radicals and/or with olefinic double bonds to ensure that a substantial degree of wasteful and deleterious ethoxylation of the vulcanisate occurs: $RH \xrightarrow{-H\cdot} R\cdot \xrightarrow{\cdot OEt} R{-}OEt$; $-C{=}C- + \cdot OEt \longrightarrow -\dot{C}{-}C(OEt)-$. Also it seems probable that a greater degree of thermal decomposition of the ethoxy-radical will occur ($CH_3{-}CH_2{-}O\cdot \longrightarrow CH_3\cdot + H{-}CHO$) than is the case with the *tert.*-butoxy-radical.

EXPERIMENTAL.

(Microanalyses by Dr. W. T. Chambers, Miss E. Farquhar, and Mrs. H. Hughes. Spectrographic observations by Dr. H. P. Koch.)

Cross-linking of 1-*Methylcyclohexene.*—The methylcyclohexene (50 g., 0·5 mol.; b. p. 109—110°/760 mm., n_D^{20} 1·4503) and di-*tert.*-butyl peroxide (18·25 g., 0·125 mol.) were heated in a Carius tube sealed under nitrogen, at 140° for 24 hours. The product (66·0 g.), a colourless mobile liquid, gave on distillation the fractions: (i) b. p. 82—110° (44·2 g.); (ii) b. p. <86°/1 mm. (0·35 g.); (iii) b. p. 86—94°/1 mm. (10·15 g.); (iv) b. p. 94—146°/1 mm. (0·45 g.); (v) b. p. 146—149°/1 mm. (3·85 g.); (vi) b. p. 203—204·5°/1 mm. (2·4 g.); (vii) a colourless, glass-like residue in the still (*ca.* 4·0 g.) which was not further investigated. Fraction (i) gave on aqueous extraction, 18·0 g. of water-soluble compounds, which consisted mainly of *tert.*-butanol (isolated as described in Part I), b. p. 82—82·5°/760 mm.; only traces of acetone were present, these being identified and determined as the 2 : 4-dinitrophenylhydrazone, m. p. 124—125° (yield 0·11 g., equiv. to 0·027 g. of acetone). The non-aqueous layer was unchanged methyl-

*cyclo*hexene (25·0 g.) which, after being dried ($CaCl_2$) and distilled over sodium, had b. p. 109—110°/760 mm., $n_D^{17\cdot5}$ 1·4510.

Fraction (iii), a colourless oily liquid, was identified as *dimethyl*dicyclo*hexenyl*. Though molecularly homogeneous, it doubtless consisted of a mixture of structural isomers. Redistillation over sodium, in nitrogen, gave a main fraction, b. p. 74—78°/0·5 mm., n_D^{20} 1·5116 [Found, for two different samples: C, 88·35, 88·55; H, 11·80, 11·65%; *M* (micro-Rast), 214, *M* (benzene), 233. $C_{14}H_{22}$ requires C, 88·35; H, 11·65%; *M*, 190]. This olefinic dimer absorbed hydrogen (Adams's catalyst) equivalent to 2·0 double bonds per mol. A larger portion (1·37 g.) in absolute ethanol (150 c.c.), when hydrogenated over palladium–charcoal (200 mg.), absorbed 305·0 c.c. of gas at N.T.P. (Calc.: 322·9 c.c.) to give the tetrahydride, dimethyldicyclohexyl. This, when distilled over sodium, gave two fractions: (i) b. p. 64—68·0°/0·5 mm., n_D^{20} 1·4827 (0·56 g.) (Found: C, 86·7; H, 13·45%); and (ii) b. p. 68·0°/0·5 mm., n_D^{20} 1·4831 (0·47 g.) (Found: C, 86·6; H, 13·5. Calc. for $C_{14}H_{26}$: C, 86·5; H, 13·5%). Both fractions were colourless mobile liquids, stable towards potassium permanganate solution and towards bromine.

Treatment of the dimeric olefin (in chloroform) at 0° with bromine led to the absorption of 2·0 mols. of halogen. The product, however, on removal of the solvent rapidly evolved hydrogen bromide and darkened; no solid tetrabromides could be isolated.

The colourless, viscous liquid forming fraction (v) was redistilled over sodium in nitrogen. It had b. p. 144—148°/1 mm., n_D^{20} 1·5339, and gave analytical values corresponding to *trimethyl*tricyclo*hexenyl* [Found: C, 88·75, 88·8; H, 11·25, 11·35%; *M* (in benzene), 268, 280, 300; unsaturation value (catalytic hydrogenation), $\overline{3}_{87}$. $C_{21}H_{38}$ requires C, 88·65; H, 11·35%; *M*, 284, $\overline{3}$]. This triolefinic trimer fraction probably contained a number of structural isomers.

Fraction (vi) was an extremely viscous, colourless semi-glass, which on distillation over sodium gave a small fraction, b. p. <186°/0·1 mm., and a main fraction, b. p. 186—192°/0·1 mm., the latter doubtless consisting of the *tetramer* (Found: C, 89·0; H, 11·35. $C_{28}H_{48}$ requires C, 88·8; H, 11·2%).

Cross-linking of 4-*Methylhept*-3-*ene*.—The olefin, prepared by dehydration of 4-methylheptan-4-ol (b. p. 70—78°/20—23 mm., n_D^{20} 1·4258) with *ca.* 0·5% of iodine, had b. p. 116—117·0°/738 mm., n_D^{20} 1·4175; infra-red spectrographic analysis indicated its main type of unsaturation to be of trialkylethylene type, R·CH:CR′R″, but there was also a small amount of the *as*-dialkylethylene type RR′C:CH_2 present, indicative of the 4-methyleneheptane isomer. Other types of unsaturation were definitely absent.

A mixture of the olefin (112 g.; 4 mols.) and the peroxide (36·5 g.; 1 mol.) was heated at 140° for 24 hours in nitrogen-filled Carius tubes. The colourless liquid product (148·0 g.) gave on distillation the fractions: (i) b. p. 80—120°/742 mm. (89·3 g.), (ii) b. p. <28°/21 mm., n_D^{20} 1·4187 (8·9 g.), and (iii) a liquid residue, n_D^{20} 1·4641 (47·9 g., equiv. to 42·7% of the original olefin), consisting entirely of olefinic hydrocarbon constituents (Found: C, 86·35, 86·1; H, 13·65, 13·65%). A portion (46·8 g.) of fraction (iii) gave on redistillation in nitrogen the following fractions: (iv) b. p. <71°/0·05 mm., n_D^{20} 1·4510 (2·0 g.); (v) b. p. 67°/0·01 mm.—72°/0·05 mm., n_D^{20} 1·4586 (25·3 g.), and a residue (vi), n_D^{20} 1·4775 (19·0 g.) (Found: C, 86·15; H, 13·4%), which was not further investigated.

The fraction (i) gave on extraction with water (300 g. + 200 g.) a mixture of water-soluble constituents (36·0 g.). Treatment of the extract with 2 : 4-dinitrophenylhydrazine solution (in 2N-hydrochloric acid) gave acetone 2 : 4-dinitrophenylhydrazone (0·32 g., equiv. to 0·08 g. of acetone). The only other water-soluble material was *tert.*-butanol (*ca.* 36·0 g., equiv. to 97·3% of the peroxide employed).

The olefin present in fractions (i) and (ii) was combined, and redistilled (in nitrogen) over sodium. It gave a monomeric fraction, b. p. 117·0—120·0°/755 mm., n_D^{20} 1·4184.

Fraction (v), a colourless oily liquid, was obviously the dimer, *hexadecadiene* [Found: C, 86·1; H, 13·6%; *M* (in benzene), 246. $C_{16}H_{30}$ requires C, 86·4; H, 13·6%; *M*, 222]. A portion of the redistilled dimer (3·1 g.), dissolved in absolute ethanol (50 c.c.), absorbed over palladium–charcoal (1·0 g.) at room temperature and pressure 535 c.c. (N.T.P.) of hydrogen, *i.e.*, 85·6% of the theoretical amount. The hexadecane so obtained was a colourless liquid, b. p. 64—67°/0·1 mm., n_D^{20} 1·4439 (2·3 g.) (Found: C, 84·9; H, 14·95. Calc. for $C_{16}H_{34}$: C, 84·85; H, 15·15%). The product was stable towards aqueous potassium permanganate for a long time.

Infra-red spectrographic examination of the recovered methylheptene revealed a higher ratio of CH_2:CRR′ to R·CH:CR′R″ than existed in the original olefin, and also showed a band at 963 cm.$^{-1}$ consistent with the presence of a trace of R·CH:CHR′, which was absent from the original olefin. In the methylheptene dimer the ratio of CH_2:CRR′ to R·CH:CR′R″ was about the same as in the original olefin. The appearance of a strong new band at 975 cm.$^{-1}$ and the broadening at the olefinic absorption band at 1640 cm.$^{-1}$ are attributed to a new form of unsaturation, RR′R″C·CH:CHR‴, not present in the original olefin. In the fully-hydrogenated methylheptene dimer the olefinic absorption in the 1650 cm.$^{-1}$ region and the strong bands at 847 cm.$^{-1}$ and 975 cm.$^{-1}$, assigned to R·CH:CR′R″ and R·CH:CHR′, respectively, were all absent.

Cross-linking of 2 : 6-*Dimethylocta*-2 : 6-*diene*.—The olefin, b. p. 56°/14 mm., n_D^{20} 1·4490 (13·8 g.; 3 mols.), was heated with the peroxide (4·9 g., 1 mol.) in a nitrogen-filled Carius tube at 140° for 24 hours. Distillation of the product (18·5 g.) gave *tert.*-butanol, together with unchanged olefin, leaving an olefinic polymer residue (6·9 g., equiv. to 50% of olefin taken), having n_D^{24} 1·4945 [Found: C, 87·3; H, 12·45%; *M* (in benzene), 362, 372]. Micro-hydrogenation of the polymer indicated a considerable reduction in unsaturation (Found: $\overline{1}_{63}$ to $\overline{1}_{45}$ per C_{10} unit). Infra-red spectrographic examination of the polymer indicated, in addition to the original type of unsaturation, appreciable amounts of RR′C:CH_2 and R·CH:CHR′ double-bond structures.

Cross-linking of Digeranyl.—The olefin (kindly supplied by Dr. D. Barnard) had b. p. 181·0—181·3°/13·5 mm., n_D^{20} 1·4831 (Found : C, 87·7; H, 12·65%; $\overline{4}_{05}$. Calc. for $C_{20}H_{34}$: C, 87·5; H, 12·5%; $\overline{4}$). A mixture of the olefin (8·22 g.; 1·5 mol.) and the peroxide (2·92 g., 1 mol.) was sealed in a Carius tube under 0·01 mm. of nitrogen, and heated at 140° for 24 hours. The product was transferred to a horizontal pot-still with a water-cooled condensing finger. Evaporative distillation at <0·01 mm. gave, first, volatile products, and then the following fractions : (i) at 50—53°, consisting mainly of digeranyl, n_D^{20} 1·4850 (1·61 g.; equiv. to 19·6% of olefin taken) [Found : C, 87·4; H, 12·6%; *M* (in benzene), 279, 295]; (ii) at 53°, a liquid, $n_D^{20\cdot2}$ 1·4859 (0·115 g.; equiv. to 1·4% of olefin taken); (iii) a colourless very viscous residue, n_D^{20} 1·5168 (6·40 g.; equiv. to 77·85% of olefin taken) [Found : C, 87·75; H, 12·1%; M (in benzene), 985, 990]. Microhydrogenation of fraction (iii) showed that it contained *ca.* 72% (Found : 71·6, 72·1%) of the unsaturation of the original digeranyl. The results of infra-red analysis of fraction (iii) were similar to those for the dimethyloctadiene residue given above.

*Cross-linking of Natural Rubber with Di-*tert.*-butyl and Diethyl Peroxide.*—The former peroxide, prepared according to Milas and Surgenor (*J. Amer. Chem. Soc.*, 1946, **68**, 205), had b. p. 109·0—110·0°/760 mm., n_D^{20} 1·3882 (Found : C, 65·7; H, 12·3. Calc. for $C_8H_{18}O_2$: C, 65·7; H, 12·4%). The diethyl peroxide, prepared by Wiley's method (U.S.P. 2,357,298/1944), had b. p. 62·5—63·5°/759·5 mm., $n_D^{18\cdot1}$ 1·3711, $n_D^{20\cdot8}$ 1·3690 (Found : C, 53·15; H, 11·25. Calc. for $C_4H_{10}O_2$: C, 53·3; H, 11·2%). Harris and Egerton (*Proc. Roy. Soc.*, 1938, *A*, **168**, 1) give b. p. 58—59°/625 mm., $n_D^{16\cdot5}$ 1·3715, and Wiley (*loc. cit.*) gives b. p. 61—65°, n_D^{23} 1·3700.

The rubber hydrocarbon used was a sample of smooth "smoked sheet" rubber. The acetone-extracted sample was prepared by extracting strips of the rubber in a nitrogen atmosphere for 24 hours, followed by drying of the swollen strip *in vacuo* for 3—5 days at 10^{-5} mm.

The experimental technique generally used was as follows : Strips of the rubber (*ca.* 4 × 0·5 × 0·1 in.) of known weight were left in contact with the calculated amounts of the appropriate peroxide in tubes sealed in an atmosphere of purified nitrogen. After 24—48 hours' contact it was assumed that even distribution of the peroxide in the rubber had been attained. The samples were quickly weighed and, while cooled in liquid air to prevent loss of peroxide, were sealed in Carius tubes in a nitrogen atmosphere of *ca.* 0·05 mm. pressure and then heated for the appropriate time (6—72 hours) and at the appropriate temperature (99·5° ± 0·5°, or 140° ± 0·5°).

The mechanical properties and equilibrium swelling constants (Q_m) in benzene (Gee, *loc. cit.*) of all the samples were measured immediately after reaction. These data are given in Tables I—III.

The volatile by-products obtained in the reaction between di-*tert.*-butyl peroxide and rubber were examined as follows :

Method 1. A sample of acetone-extracted rubber was dried for 4 days at 10^{-5} mm. and then immediately analysed (Found : C, 86·3; H, 11·45; O,* 0·98, 0·965; ash, 0·25%). This sample was heated with di-*tert.*-butyl peroxide (51·5 g./100 g. of rubber) for 6 hours at 140°. The liquid which separated from the product was shown to be mainly *tert.*-butanol, together with some acetone, but no peroxide. The rubber derivative (a hard brittle solid having no rubber-like properties) was acetone-extracted and dried for 7—9 days at 10^{-5} mm. (Found : C, 87·3, 86·6; H, 11·3, 11·55; O,* 1·32, 1·32; ash, 0·95%).

Method 2. A sample of rubber (17·0 g.), as in (1), was allowed to imbibe the peroxide (8·2 g.) in an atmosphere of nitrogen during 2 weeks, the resulting mixture then being heated under nitrogen for 6 hours at 140°. The liquid product (5·8 g.), which separated out after the reaction, was pumped off at 1 mm. pressure and condensed in a liquid-air trap. It was a colourless liquid boiling entirely over the range 56—80° and was shown to consist of a mixture of acetone (36·3% of peroxide taken), determined and identified as its 2 : 4-dinitrophenylhydrazone, m. p. 124—125° (mixed m. p. 125°), and *tert.*-butanol (equiv. to 41·1% of peroxide taken), identified as its phenylurethane, m. p. and mixed m. p. 136°. No unchanged peroxide was found.

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[*Received, July 26th*, 1950.]

* Direct determination.

31. *Radical Mechanisms in Saturated and Olefinic Systems. Part III. The Reaction of Hydroxyl Radicals with Olefins.*

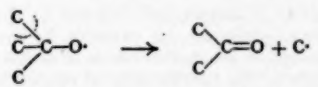
By E. H. Farmer and C. G. Moore.

The hydroxyl radicals and *tert.*-butoxy-radicals formed by the thermal decomposition of *tert.*-butyl hydroperoxide have been brought into reaction with *cyclo*hexene and with 1-methyl*cyclo*hexene at 140° in order to determine the characteristic reactivities towards olefinic carbon chains of the hydroxyl radicals.

The olefins are dehydrogenated at their α-methylene groups, and the olefin radicals so formed pass into dehydro-dimeric and to some extent into higher dehydro-polymeric forms which are mostly oxygenated. The bulk, but not quite all, of the dehydrogenation is accomplished by the *tert.*-butoxy-radicals, the hydroxyl radicals being mostly expended in oxygenating the monomeric and polymeric olefin forms. Considerable yields of α-hydroxy- and α-keto-*cyclo*hexenes and -di*cyclo*hexenyls are formed from *cyclo*hexene, together with higher oxygenated polymeric forms, and comparable products are obtained from 1-methyl*cyclo*hexene, although here the unsymmetrical character of the resonating olefin radicals causes isomerism. The mechanism of hydroxylic and double hydroxylic substitution at α-methylenic positions is discussed. Only to a relatively small extent are hydroxyl radicals added (in pairs) at olefinic double bonds to give 1 : 2-diols, and it is notable that to no observable extent do they react additively with such double bonds to give epoxide groupings.

The thermal decomposition of a saturated alkyl hydroperoxide (R–OOH $\longrightarrow$ R–O· + ·OH) may be expected to yield a pair of radicals of very dissimilar reactivity. Thus when *tert.*-butyl hydroperoxide is decomposed in presence of an olefin the dehydrogenating action which characterises the moderately stabilised (not intensely electrophilic) *tert.*-butoxy-radical to almost complete exclusion of other reactivities is hardly likely to apply with equal exclusiveness to the little stabilised (highly electrophilic) hydroxyl radical. It was interesting, therefore, to discover to what extent (if any) the hydroxyl radical from *tert.*-butyl hydroperoxide is capable of reacting with a simple olefin in the various ways which may (with more or less justification) be suspected to be open to it. These are: (1) Dehydrogenation at α-methylene groups to give olefin radicals: $RH + {\cdot}OH \longrightarrow R{\cdot} + H_2O$. (2) Union with α-methylenic olefin radicals to give alcohols: $R{\cdot} + {\cdot}OH \longrightarrow R{\cdot}OH$. (3) Addition to double bonds in pairs to give saturated glycols: $C{=}C + 2\,{\cdot}OH \longrightarrow C(OH){-}C(OH)$. (4) Re-hydroxylation of >CH(OH) groups to give ketones $>CH{-}OH \xrightarrow[(a)]{-H} >\dot{C}(OH) \xrightarrow[(b)]{\cdot OH} >C(OH)_2$. (5) Addition to double bonds singly to give epoxides. The first of these ways appears from all present information to be open to all radicals except those of the most outstanding stability, and the second is a feasible second stage for a process of substitutive hydroxylation.* The third, fourth, and fifth ways appear to be possible in view of the frequent formation of glycols, ketones, and epoxides during the autoxidation of olefins.

Careful investigation of the decomposition of *tert.*-butyl hydroperoxide (1 mol.) in presence of a large excess of *cyclo*hexene (6 mols.) gives results which are entirely compatible with the simultaneous reaction on the olefin of *tert.*-alkoxyl and hydroxyl radicals. The *tert.*-alkoxy-group clearly acts as a dehydrogenating agent, since it reappears as *tert.*-butanol, only under-



going thermal breakdown to acetone to a minute extent. The full list of products identified, and their yields, are given in the table.

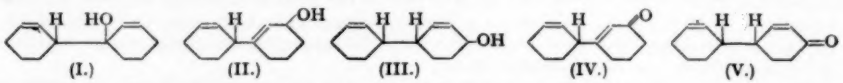
* Such substitutive hydroxylation is probably not the main path to the formation of olefinic alcohols in olefin autoxidation, in which the thermal scission of hydroperoxides (R–O–OH) may be followed by hydrogenation of the alkoxy-group and conceivably also by the substitution $RO{\cdot} + {\cdot}OH \longrightarrow ROH + {\cdot}O{\cdot}$.

Interaction of cyclo*hexene* (328 *g.*, 4·0 *g.-mols.*) *with* tert.*-butyl hydroperoxide* (60 *g.*, 0·67 *g.-mol.*) (140°; 24 *hours*).

Products.	G.	G.-mols.	Products.	G.	G.-mols.
tert.-Butanol	46·7	0·62	*trans-cyclo*Hexane-1 : 2-diol ...	1·25	0·011
Water	3·4	0·19	*cyclo*Hexenyl*cyclo*hexenol(s) ...	$>$5·2	$>$0·03
Acetone	0·05	$0{\cdot}0_2$86	*cyclo*Hexenyl*cyclo*hexenone(s)	$>$0·92	$>$0·0252
*cyclo*Hex-2-enol	*ca.* 17·4	~0·18	Ter*cyclo*hexenyl (s)	*ca.* 2·7	~0·011
*cyclo*Hex-2-enone	*ca.* 3·1	~0·032	Residue	5·1	—
Di*cyclo*hexenyl	$>$28·25	$>$0·175			

In considering the origin of the various products it is impossible to distinguish between the dehydrogenation effected by the *tert.*-butoxy- and by the hydroxyl radicals, but there can be no doubt that some part of the dehydrogenation of the olefin (reaction 1, above) must have been accomplished by the hydroxyl radicals since the yield of water formed in the reaction is appreciable—considerably higher, indeed, than can be accounted for by mere elimination of water during ketone formation [*i.e.*, at stage 4(*b*) of the reaction paths listed above]. Most of the dehydrogenation, however, must be attributed to the *tert.*-butoxy-radicals which pass thereby into *tert.*-butanol, since, not only is the degree of recovery of the latter actually achieved high (95%), but the degree to which the *tert.*-butoxy-radicals have been expended in thermal decomposition (to give acetone) is trivial and that of their coupling with olefin radicals to give ethers, comparable with reaction 2($R\cdot + Bu^tO\cdot \longrightarrow R{-}OBu^t$), insignificant. The dehydrogenation has been followed by extensive coupling of the resulting olefin radicals to give first di- and then ter-*cyclo*hexenyl, etc. Correspondingly, most of the hydroxyl radicals appear to have been used in oxygenation of the olefin—principally in converting olefin radicals into olefinic alcohols and thence (in part) into αβ-unsaturated ketones: indeed, only to a relatively small extent have they been expended in direct addition to double bonds to give (saturated) *cyclo*hexane-1 : 2-diol, and to no recognisable extent at all have they contributed to the formation of epoxides. The apparent entire absence of *cyclo*hexene epoxide from the reaction product suggests that the epoxides which are so frequently formed in the autoxidation of olefinic materials cannot result from any very simple interaction of hydroxyl radicals with double bonds, and may in fact depend for their formation on the transient liberation of atomic oxygen from decomposing $-OOH$ groups or $-OO-$ radicals.

The capacity for advanced oxygenation (*e.g.*, beyond simple substitutive hydroxylation) shown by the hydroxyl groups is confined to ketone formation, the fairly abundant *cyclo*hex-2-enol in the reaction product being accompanied by a moderate yield of the corresponding ketone, *cyclo*hex-2-enone. With respect to the dimer alcohols and ketones formed, which probably spring in the main from the already dehydro-dimerised olefin, no allocation of specific formulæ can be made, since the separation and identification of the individual isomers was not attempted. Previous results in this series (see Part I), however, indicate that substitution at the tertiary carbon atoms in di*cyclo*hexenyl may be sufficiently hindered sterically to permit reaction to occur in quite important degree at secondary as well as tertiary α-methylenic positions. Such substitutive hydroxylation, together with the occurrence of allylic resonance

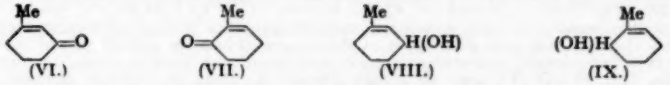


(I.) (II.) (III.) (IV.) (V.)

in the tertiary radicals, will be likely to give the alcohols (I—III) and the ketones (IV and V). Corresponding, but less abundant, hydroxy- and keto-derivatives of "trimeric" (and possibly higher) olefinic forms were probably present in the highest-boiling portion of the product, but were not isolated.

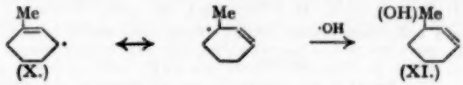
Finally, no significant amount of oxygenation carried to the stage of chain scission has occurred in the *cyclo*hexene ring—produced, for example, by the further attack of hydroxyl radicals at the α-methylenic groups or the double bonds of first-formed ketones. This feature, however, appears to be due only to the insufficiency of reagent radicals, since supplementary experiments in which *cyclo*hexanol (1 mol.) and *cyclo*hex-2-enol (0·41 mol.) were in turn heated with *tert.*-butyl hydroperoxide (1 mol.) at 130° gave in both cases much of the corresponding (saturated or unsaturated) ketone, and an appreciable amount of carboxylic acid. The acid from *cyclo*hexanol was found to be adipic acid, thus emphasizing that substitutive attack by hydroxyl groups occurs very readily at the α-carbon atoms of saturated secondary alcohols, and then at the α-methylene groups of the resulting ketones.

A similar, but less complete examination of the action of thermally decomposing *tert.*-butyl hydroperoxide on 1-methyl*cyclo*hexene at 140° was carried out. In this example the presence of the methyl group in the olefin molecule produced, owing to its destruction of the molecular



(VI.) (VII.) (VIII.) (IX.)

symmetry, appropriate isomerism among the hydroxy- and keto-derivatives of the olefins, and doubtless (although this was not investigated) also among the " dimeric " and higher " polymeric " olefins themselves. Amongst the simple products, the isomeric cyclic ketones (VI) and (VII) were easily identified, as also the corresponding, more abundant, alcohols (VIII) and (IX), which passed on oxidation into (VI) and (VII). The third theoretically possible



(X.) (XI.)

(tertiary) *cyclo*hexenol (XI) and/or derivatives thereof may well have been present, but were not actually sought.

Experimental.

(Microanalyses by Dr. W. T. Chambers, Miss E. Farquhar, and Mrs. H. Hughes. Spectrographic observations by Dr. H. P. Koch.)

Reaction of tert.-*Butyl Hydroperoxide with* cyclo*Hexene.—tert.*-Butyl hydroperoxide was prepared according to Milas and Surgenor (*J. Amer. Chem. Soc.*, 1946, **68**, 205). The final product, after drying ($MgClO_4$), had b. p. 37·5—38·0°/20 mm., n_D^{20} 1·4004, n_D^{25} 1·3980 (Milas and Surgenor, *loc. cit.*, give n_D^{20} 1·4013, and Milas and Perry, *loc. cit.*, give b. p. 33—34°/17 mm., n_D^{25} 1·3983).

A mixture of *cyclo*hexene (328 g., 4 mols.) and the hydroperoxide (60 g., 0·67 mol.) was heated at 140° (±1°) for 24 hours in nitrogen-filled Carius tubes. The product (386·2 g.) separated into two layers, a small aqueous lower one and a large yellow upper one. Both layers were submitted to fractional distillation in nitrogen. A large volatile fraction (i) b. p. 66·0—82·5°/750 mm. (257·2 g.) first distilled, and a second volatile fraction (ii), consisting of *cyclo*hexene (n_D^{20} 1·4460; 47·0 g.), was removed from the residue by spontaneous distillation at 10 mm. pressure into a liquid-air trap. The residual fraction (iii) was a light yellow oxygen-containing liquor (78·4 g.) [Found: C, 81·25; H, 11·05; O (by diff.), 7·7; OH (Zerewitinoff), 6·75, 6·85, 6·95; O (as OH), 6·35—6·54%]. Distillation of fraction (iii), in nitrogen, gave the fractions (iv), b. p. 53—62·5° (mainly 62·0—62·5°)/10 mm., n_D^{20} 1·4740 (23·2 g.); (v) b. p. 62·5°/10 mm.—63°/0·6 mm., n_D^{20} 1·4798 (5·05 g.); (vi) b. p. 63—68°/0·6—0·7 mm., n_D^{20} 1·5000 (29·5 g.), and (vii) a residual viscous yellow liquid (16·7 g.). Redistillation of fraction (vii) from a smaller still gave (viii) b. p. 72—106°/1 mm., n_D^{20} 1·5080 (0·68 g.); (ix) b. p. 106—132°/1 mm., n_D^{20} 1·5210 (6·55 g.); (x) b. p. 132—142°/1 mm., n_D^{20} 1·5319 (2·7 g.); and (xi) a residual viscous orange liquid, undistillable at 200° (bath temp.)/1 mm., n_D^{20} 1·5455 (5·1 g.).

The fraction (i) consisted of a mixture of *cyclo*hexene, *tert.*-butanol (*ca.* 46·7 g.; equiv. to 94·8% of hydroperoxide taken), acetone (0·05 g.), and water (3·4 g.). The *tert.*-butanol and acetone were identified and determined as previously described. An approximate estimate of the water formed in the reaction was made by shaking the bulk fraction with anhydrous potassium carbonate (30·0 g.); the increase in weight of the latter amounted to 3·4 g. The *cyclo*hexene present in fractions (i) and (ii was combined, dried ($CaCl_2$), and distilled over sodium, in nitrogen. It had b. p. 82·5°/750 mm., n_D^{25} 1·4461.

The fraction (iv), a colourless oily liquid, consisted of *cyclo*hex-2-enol and a smaller amount of *cyclo*hex-2-enone, together with a little olefinic material (probably di*cyclo*hexenyl) which repeated refractionation failed to remove [Found: C, 74·6; H, 10·65; OH (Zerewitinoff), 13·0. Calc. for $C_6H_{10}O$: C, 73·4; H, 10·3; OH, 17·35%. Calc. for C_6H_8O: C, 75·0; H, 8·4%]. The *cyclo*hex-2-enol was characterised by its α-naphthylurethane, m. p. and mixed m. p. 156° (Found: C, 76·05; H, 6·35; N, 5·15, 5·2. Calc. for $C_{17}H_{17}O_2N$: C, 76·4; H, 6·4; N, 5·25%). The *cyclo*hex-2-enone was characterised by its 2 : 4-dinitrophenylhydrazone, which separated as deep red-orange needles from light petroleum (b. p. 100—120°). It had m. p. and mixed m. p. 162—163° (Found: C, 52·2; H, 4·45; N, 20·5. Calc. for $C_{12}H_{12}O_4N_4$: C, 52·2; H, 4·4; N, 20·3%). Quantitative determination of the ketone content of fraction (iv) by the method of Iddles, Low, Rosen, and Hart (*Ind. Eng. Chem. Anal.*, 1939, **11**, 102) indicated that 13·35% of it consisted of *cyclo*hex-2-enone. The percentage of hydroxylic and carbonyl oxygen (12·23 + 2·33) derivable from the foregoing analyses of fraction (iv) shows a total OH + CO oxygen content therein of 14·46%. This total agrees well with the oxygen content of 14·75% (diff. value) obtained by elementary methods of analysis of the fraction, and so indicates that no substantial proportions of other oxygenated groups were present. Catalytic hydrogenation of a portion of (iv) with palladium–charcoal in absolute ethanol gave a product which by treatment with 2 : 4-dinitrophenylhydrazine yielded *cyclo*hexanone 2 : 4-dinitrophenylhydrazone as orange-yellow plates from ethanol, m. p. and mixed m. p. 156—158° (Found: C, 52·15; H, 5·2. Calc. for $C_{12}H_{14}O_4N_4$: C, 51·8; H, 5·05%).

Ultra-violet spectrographic analysis of fraction (iv) showed an absorption maximum at λ 2250 A., ε = 1350, compatible with *ca.* 10—13% of *cyclo*hex-2-enone (cf. Cooke and Macbeth, *J.*, 1938, 1408; Birch, *J.*, 1946, 593; Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123).

The fraction (vi), a colourless oily liquid, deposited on cooling crystals of *trans-cyclo*hexane-1 : 2-diol, m. p. 102—104° (1·25 g.) (Found : C, 62·25; H, 10·4. Calc. for $C_6H_{12}O_2$: C, 62·05; H, 10·4%). The liquid residue consisted of di*cyclo*hexenyl, contaminated with a little oxygenated material (Found : C, 87·85; H, 11·3%). Repeated distillation of the impure olefin over sodium proved ineffective for removal of the contaminant; repeated extraction with water was more successful, giving a slightly impure olefin, b. p. 61—62°/0·5 mm., n_D^{20} 1·5082 (Found : C, 88·3; H, 11·3%); the best result was obtained by chromatography of a solution of the *cyclo*alkene in light petroleum (b. p. 60—80°) through activated alumina, whereby an almost pure *cyclo*alkene, b. p. 69—71°/1 mm., n_D^{16} 1·5099, was obtained [Found : C, 88·65, 88·25; H, 11·6, 11·3%; *M* (micro-Rast), 159, 160; $\overline{I}_{1\cdot99}$ (by catalytic hydrogenation) Calc. for $C_{12}H_{18}$: C, 88·8; H, 11·2%; *M*, 162; $\overline{3}$]. The oxygenated impurity, obtained by elution of the chromatogram with absolute ethanol, proved to be *trans-cyclo*hexane-1 : 2-diol, m. p. 104° (Found : C, 62·4; H, 10·15%). Addition of bromine to a representative sample of the *cyclo*alkene in the way previously described gave the two known tetrabromides of di*cyclo*hexenyl of m. p.s 159—160° (Found : C, 30·15; H, 3·75. Calc. for $C_{12}H_{18}Br_4$: C, 29·9; H, 3·75%) and 189—191° (Found : C, 29·6; H, 3·85%).

The fraction (ix) was a colourless viscous highly-oxygenated liquid (Found : C, 81·6; H, 10·3%). A portion of this (2·7 g.) gave on re-fractionation the following sub-fractions : (*a*) b. p. <87·5°/0·05 mm., n_D^{20} 1·5110 (0·4 g.); (*b*) b. p. 87·5—90·0°/0·04 mm., n_D^{20} 1·5160 (1·0 g.); (*c*) b. p. 90·0—105°/0·04 mm., n_D^{20} 1·5253 (1·0 g.). The fraction (*b*) contained, as indicated by the analytical data, *ca.* 80% of cyclo*hexenyl*cyclo*hexenol*, $C_{12}H_{18}O$, and *ca.* 14% of cyclo*hexenyl*cyclo*hexenone* [Found : C, 79·9; H, 10·25; OH (Zerewitinoff), 7·6. $C_{12}H_{18}O$ requires C, 80·85; H, 10·2; OH, 9·55%]; $\lambda_{max.}$ 2260 A., ε = 1400. A similar sample had b. p. 110—126°/1 mm., n_D^{17} 1·5160 [Found : C, 80·75; H, 10·05%; $\overline{I}_{1\cdot7}$ (microhydrogenation)]. Fraction (*c*) was a mixture of the alcohol and ketone with a little higher-boiling olefin (Found : C, 81·6; H, 10·35%). Owing to the small amount of the alcohol–ketone mixture isolated, no structural investigation was possible.

Fraction (x) was shown to be mainly ter*cyclo*hexenyl with a little oxygenated material as impurity. On redistillation over sodium, a main fraction was obtained, b. p. 108—110°/0·5 mm., n_D^{20} 1·5328 (Found : C, 88·0; H, 10·85. Calc. for $C_{18}H_{24}$: C, 89·2; H, 10·8%).

The residue (xi), a mixture of high-boiling alcohols and olefins (Found : C, 85·1; H, 10·5%), was not further examined.

Reaction of tert.-*Butyl Hydroperoxide with* cyclo*Hexanol.*—*cyclo*Hexanol, b. p. 64°/17 mm. (10 g., 1 mol.) and the hydroperoxide (9·0 g., 1 mol.) were heated under reflux at 130° for 24 hours. On fractionation, the product gave (i) *tert.*-butanol, b. p. 80—83°/747 mm. (5·5 g., equivalent to 74·3% of the peroxide taken), (ii) a fraction, b. p. 140—156°/747 mm. (9·8 g.), containing *cyclo*hexanone (19%), determined and identified as its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 157—158° (Found : C, 52·0; H, 5·35. Calc. for $C_{12}H_{14}O_4N_4$: C, 51·8; H, 5·05%), and (iii) a residue (2·0 g.) containing a small amount of adipic acid which after crystallisation from ether had m. p. 147—148·5°.

Reaction of tert.-*Butyl Hydroperoxide with* cyclo*Hex-2-enol.*—The alcohol (b. p. 162—165°/752 mm.; *a*-naphthylurethane, m. p. 156°; 4·0 g.) and hydroperoxide (9·0 g.) were heated under reflux at 130° for 24 hours. Fractionation of the product gave (i) *tert.*-butanol (3·3 g., equivalent to 44·6% of the peroxide taken), (ii) unchanged peroxide (3·6 g.), (iii) a fraction, b. p. 150—163° (3·55 g.), containing *ca.* 18% of *cyclo*hex-2-enone, determined and identified as its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 158—160° (Found : C, 52·3; H, 4·5. Calc. for $C_{12}H_{12}O_4N_4$: C, 52·2; H, 4·4%).

Reaction of tert.-*Butyl Hydroperoxide with* 1-*Methyl*cyclo*hexene.*—A mixture of the olefin (144 g., 1·5 mols.) and the hydroperoxide (45 g., 0·5 mol.) was heated at 140° for 24 hours in nitrogen-filled Carius tubes. The product (187·2 g.) was a bright yellow liquid which on fractionation gave the following fractions : (i) b. p. 78—112°/735 mm. (104·7 g.), containing a small aqueous layer; (ii) evaporated spontaneously into a liquid-air trap at 13 mm. (7·0 g.); (iii) b. p. <53°/13 mm., n_D^{20} 1·4520 (20·5 g.); (iv) b. p. 53—77° (mainly 67—77°)/13 mm. (14·2 g.); and (v) a yellow viscous residue, not further investigated.

The fraction (i) contained water-soluble and water-insoluble portions. The former 37·1 g.) consisted mainly of *tert.*-butanol, together with a small amount of water and a trace of acetone; the latter, like fractions (ii) and (iii), consisted of unchanged *cyclo*alkene, and these when combined, dried ($CaCl_2$), and distilled in nitrogen over sodium gave a main fraction, b. p. 107—108°, n_D^{20} 1·4501 (73·6 g.).

The fraction (iv), a colourless oily liquid, was a mixture of methyl *cyclo*hexenols and methyl*cyclo*hexenones (Found : C, 76·1; H, 10·55. Calc. for $C_7H_{12}O$: C, 74·95; H, 10·7%). Ultra-violet spectrographic analysis disclosed a selective absorption band at λ 2310 A., ε = 1200, consistent with the presence of ~12% of conjugated methyl*cyclo*hexenones.

Treatment of a portion (0·5 g.) of this fraction with 2 : 4-dinitrophenylhydrazine in absolute ethanol gave a mixture of deep red dinitrophenylhydrazones (0·25 g.); these (25 mg.), dissolved in light petroleum (b. p. 40—60°) (150 c.c.), were chromatographed on a column of alumina (30 g.; 600 × 9 mm.), and became adsorbed in two distinct bands. The upper band consisted of 3-methyl*cyclo*hex-2-enone dinitrophenylhydrazone (4·4 mg.), m. p. 168—170°, and the lower band contained 2-methyl*cyclo*hex-2-enone dinitrophenylhydrazone (9·7 mg.), m. p. 198—200°, mixed m. p. 199—201°.

To a further portion (6·0 g.) of (iv) in glacial acetic acid (10 c.c.) there was added with cooling a solution of chromic anhydride acid (4·0 g.) in 75% aqueous acetic acid (10 c.c.). The oxidation was completed by warming the mixture on the water-bath for 30 minutes. The ketonic portion was extracted with ether (200 c.c.), and the ethereal layer neutralised with saturated sodium hydrogen carbonate

solution and then dried ($CaCl_2$). After removal of the solvent the product was distilled, giving a fraction (i) b. p. 62—70°/13 mm., n_D^{20} 1·4672 (2·2 g.), and a higher-boiling residue (ii) (1·2 g.). The ketone content of fraction (i), determined as its dinitrophenylhydrazone, was 64%. Chromatographic separation of the mixed dinitrophenylhydrazones (30 mg.) as described above gave the dinitrophenylhydrazones of 2-methyl*cyclo*hex-2-enone (12·1 mg.) and 3-methyl*cyclo*hex-2-enone (5·0 mg.).

The three papers, of which this is the last, form part of a programme of fundamental research undertaken by the Board of The British Rubber Producers' Research Association. The authors thank Professor G. R. Clemo, F.R.S., for his interest and for affording facilities (1945—1947) at King's College, Newcastle-on-Tyne, during the course of part of this work.

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32. *The Electrolytic Dissociation of Zinc Sulphate, Copper Sulphate, and Zinc Malonate in Mixed Solvents.*

By J. C. JAMES.

Conductivity measurements are reported for dilute solutions of zinc sulphate, copper sulphate, and zinc malonate in binary mixtures of water with dioxan, acetone, ethylene glycol, and ethanol at 25°. Dissociation constants have been derived, and the variation of dissociation constant with dielectric constant is discussed. It is suggested that dissociation constants become less dependent on dielectric constant when association is not completely determined by Coulomb forces. Conductivity measurements are also reported for aqueous zinc malonate solutions at 25° and 30°; dissociation constants have been calculated and thence ΔH, ΔG, and ΔS for dissociation.

RECENTLY (James, *J.*, 1950, 1094), conductivity measurements on a 3–3 valency type electrolyte, lanthanum ferricyanide, were reported for a series of mixed solvents, and it was shown that, for the water-rich mixtures studied, the variation in dissociation constant with dielectric constant could be accounted for satisfactorily by the Bjerrum ion-pair treatment. This work has now been extended to salts of the 2–2 valency type, and measurements are reported for solutions of zinc sulphate, copper sulphate, and zinc malonate in binary mixtures of water with dioxan, acetone, ethylene glycol, and ethanol at 25°. With zinc sulphate and copper sulphate, the stable electronic structures of the ions indicate that association is purely electrostatic, to give ion pairs. Zinc malonate, however, behaves as a comparatively weak electrolyte in aqueous solution, and it has been suggested (Ives and Riley, *J.*, 1921, 1998; Bjerrum, *Chem. Reviews*, 1950, **46**, 381) that a chelate ring structure is involved. The purpose of the present investigation was to compare dissociation-constant data for these salts in mixed solvents, and thereby to obtain information as to the nature of the association involved. Also, as the dissociation constant of zinc malonate can be determined with considerable accuracy by the conductivity method, it is possible to obtain values of ΔH and ΔS for the dissociation process from measurements at different temperatures. Conductivity measurements have therefore been made on dilute aqueous zinc malonate solutions at 25° and 30°.

EXPERIMENTAL.

The experimental procedure and methods used for solvent purification have been described previously (James, *loc. cit.*). Zinc malonate was prepared by the method of Ives and Riley (*loc. cit.*) (Found: Zn, 32·1. Calc. for $C_3H_2O_4Zn,2H_2O$: Zn, 32·1%). Pure zinc sulphate and copper sulphate were prepared by recrystallising AnalaR-quality specimens twice from conductivity water, and drying them over the partly dehydrated salts.

DISCUSSION.

Aqueous Zinc Malonate Solutions.—The results for aqueous zinc malonate solutions at 25° and 30° are given in Table I. At 25°, combination of the value $\Lambda_0(Zn) = 53{\cdot}0$ given by Owen and Gurry (*J. Amer. Chem. Soc.*, 1938, **60**, 3074) for the zinc ion with Jeffery and Vogel's (*J.*, 1935, 21) value of 64·7 for the malonate ion leads to $\Lambda_0 = 117{\cdot}7$ for the conductivity at infinite dilution. Application of the method given by Davies (*J.*, 1933, 645) for the extrapolation of experimental results for incompletely dissociated electrolytes gives $\Lambda_0 = 117{\cdot}6$, in good agreement. At 30°, application of this method gives $\Lambda_0 = 130{\cdot}7$ and, although no independent

value can be obtained for comparison, the excellent agreement at 25° suggests that the use of this method at 30° is permissible. For the purpose of comparison of dissociation constants the values $\Lambda_0^{25} = 117{\cdot}6$ and $\Lambda_0^{30} = 130{\cdot}7$ were adopted, the limiting Onsager and Debye–Hückel equations then becoming

$$\Lambda = \alpha[117{\cdot}6 - 228{\cdot}0I^{\frac{1}{2}}], \quad -\log f_{\pm}^{\ 2} = 4{\cdot}074I^{\frac{1}{2}} \text{ at } 25°$$
$$\Lambda = \alpha[130{\cdot}7 - 255{\cdot}7I^{\frac{1}{2}}], \quad -\log f_{\pm}^{\ 2} = 4{\cdot}113I^{\frac{1}{2}} \text{ at } 30°$$

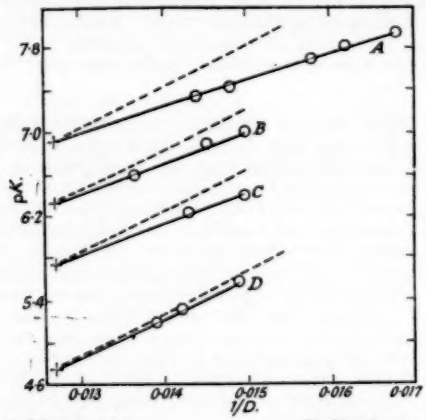
where α is the degree of dissociation. The ionic strength, I, is given by $I = 2\alpha c$, where c is the concentration in g.-equivs./l. Values of α and dissociation constants have been derived for each point from the equations

$$\log K = \log [\alpha^2 c/2(1 - \alpha)] - 4{\cdot}074I^{\frac{1}{2}} \text{ at } 25°$$
and
$$\log K = \log [\alpha^2 c/2(1 - \alpha)] - 4{\cdot}113I^{\frac{1}{2}} \text{ at } 30°$$

The mean values are: at 25°, $K = 1{\cdot}793 \times 10^{-4}$, and at 30°, $K = 1{\cdot}644 \times 10^{-4}$, the average deviation at each temperature being $0{\cdot}004 \times 10^{-4}$. From these dissociation constants it is found that $\Delta H = -3{\cdot}06$ kcals. between 25° and 30°, $\Delta G_{298{\cdot}1} = 5110$ cals. and $\Delta S_{298{\cdot}1} = -27{\cdot}5$ cals./°c. for the dissociation process. These values for ΔH and ΔS are of the same order but slightly greater numerically than the corresponding values obtained by Davies and James (*Proc. Roy. Soc.*, **1948**, *A*, **195**, 116) for lanthanum ferricyanide ion pairs ($\Delta H = -2{\cdot}0_0$ kcals.,

FIG. 1.

Variation of dissociation constant with dielectric constant for zinc malonate in mixed solvents.



A, Dioxan–water. *B*, Glycol–water.
C, Ethanol–water. *D*, Acetone–water.

Results for ethanol–, glycol–, and dioxan–water mixtures have been displaced vertically by 1·0, 1·6, *and* 2·2 p*K units respectively, for clarity.*

TABLE I.

Conductivity of aqueous zinc malonate solutions.

Run.	$10^6\kappa_{H_2O}$.	10^4c.	$10^2c^{\frac{1}{2}}$.	Λ.	10^4K.	Run.	$10^6\kappa_{H_2O}$.	10^4c.	$10^2c^{\frac{1}{2}}$.	Λ.	10^4K.
		At 25°.						*At* 30°.			
1	0·446	1·9934	1·412	84·23	1·798	1	0·277	2·6881	1·640	85·76	1·636
		3·8952	1·974	72·07	1·803			6·5578	2·561	67·26	1·644
		7·0068	2·647	60·99	1·796			9·6489	3·106	59·52	1·644
		9·9980	3·159	54·56	1·793			13·632	3·692	52·94	1·640
		13·785	3·713	48·97	1·789			19·735	4·442	46·43	1·640
2	0·351	3·4262	1·851	74·34	1·790	2	0·246	2·1674	1·472	90·31	1·635
		6·2112	2·492	63·21	1·794			4·9798	2·231	73·08	1·652
		10·767	3·281	53·21	1·792			9·0854	3·014	60·74	1·647
		15·684	3·960	46·83	1·788			13·254	3·641	53·47	1·642
		22·222	4·714	41·38	1·788			18·473	4·299	47·57	1·641

$\Delta S_{298\cdot1} = -23\cdot9$ cals./°c.), although the experimental uncertainty is possibly too great for any significance to be attached to such differences.

Mixed Solvents.—The results for zinc malonate, zinc sulphate, and copper sulphate in mixed solvents are given in Table II. Values for Λ_0 have been derived by Davies's method (*loc. cit.*),

TABLE II.

(A) *Conductivity of zinc malonate in mixed solvents.*

Dioxan–water.

10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.
10·30% Dioxan (1).		12·37% Dioxan (2).		17·11% Dioxan (3).		18·98% Dioxan (4).		21·30% Dioxan (5).	
2·7327	48·69	2·3835	44·15	4·1747	28·75	1·7430	35·16	4·5181	20·947
6·6686	36·75	5·2049	35·02	9·8272	20·515	3·2999	27·93	7·3221	17·138
10·813	30·80	8·1200	29·96	15·176	17·144	5·2249	23·26	12·385	13·697
16·034	26·44	11·728	26·09	21·076	14·955	8·0178	19·524	17·977	11·688
22·146	23·27	15·889	23·16	31·152	12·710	10·804	17·217	23·961	10·356

Acetone–water.

10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.
11·83% Acetone (6).		14·41% Acetone (7).		19·78% Acetone (8).	
2·9613	43·26	2·5418	39·81	4·6885	24·00
6·2507	33·58	5·5384	30·34	8·9471	18·404
10·726	27·35	8·9340	25·24	12·460	16·040
15·041	23·94	16·022	19·926	15·697	14·553
20·192	21·28	23·135	17·134	19·861	13·184

Ethanol–water.

10^4c.	Λ.	10^4c.	Λ.
13·71% Ethanol (13).		20·50% Ethanol (14).	
5·1030	27·55	9·2507	13·408
9·5415	21·74	11·834	12·151
12·161	19·789	14·568	11·155
15·546	17·936	17·585	10·321
19·407	16·395	21·357	9·533

Glycol–*water.*

10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.
18·65% Glycol (9).		26·41% Glycol (10).		33·17% Glycol (11).		39·57% Glycol (12).	
2·8790	42·34	4·5674	26·68	6·7743	17·060	8·6244	11·391
5·3867	34·82	9·5145	20·38	8·9948	15·301	10·857	10·380
9·8274	28·20	11·844	18·736	11·411	13·938	14·154	9·297
12·255	25·92	16·366	16·508	14·461	12·675	16·649	8·724
15·336	23·78	19·801	15·307	17·051	11·856	21·855	7·806

(B) *Conductivity of zinc sulphate in mixed solvents.*

Dioxan–water.

10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.
17·26% Dioxan (15).		25·52% Dioxan (16).		30·83% Dioxan (17).	
2·4537	88·01	1·9084	72·60	2·2514	58·41
5·5810	81·08	3·6704	66·59	3·9133	52·81
8·7159	76·41	5·9643	61·36	6·0127	48·11
12·772	71·95	9·3663	56·14	8·1264	44·72
17·985	67·67	11·8599	53·31	12·059	40·32

Acetone–water.

10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.
10·95% Acetone (18).		13·67% Acetone (19).		26·33% Acetone (20).	
1·7956	100·93	1·8519	89·27	2·5469	72·34
4·4583	95·26	4·1558	83·90	4·6201	66·77
7·1500	91·25	6·6064	79·82	6·9280	62·39
10·087	87·72	9·745	79·85	9·590	58·64
14·183	83·47	12·517	73·09	12·642	55·29

Glycol–water.

10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.
27·11% Glycol (21).		39·14% Glycol (22).		52·20% Glycol (23).	
4·2167	64·21	3·3558	46·91	3·6641	31·23
6·8957	61·67	5·5285	44·95	9·0800	27·84
10·616	58·92	9·0525	42·55	11·783	26·68
14·244	56·84	12·711	40·63	15·411	25·45
17·630	55·23	15·913	39·27	19·453	24·34

Ethanol–water.

10^4c.	Λ.	10^4c.	Λ.
18·01% Ethanol (24).		24·99% Ethanol (25).	
1·4817	71·60	2·7452	57·47
2·5575	69·23	4·0232	54·91
3·7938	67·01	5·8235	52·14
5·5262	64·48	8·2938	49·18
6·4600	63·32	10·3623	47·21

(C) *Conductivity of copper sulphate in mixed solvents.*

10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.	10^4c.	Λ.
23·43% Dioxan (26).		20·19% Acetone (27).		35·03% Glycol (28).		21·17% Ethanol (29).	
2·3673	78·28	2·1380	81·99	4·3105	50·84	2·0445	62·86
4·2966	71·93	3·5929	77·88	5·8384	49·58	3·9848	58·85
6·3692	67·12	5·5829	73·55	7·9846	48·00	6·3738	55·17
8·5847	63·25	9·2403	67·82	10·954	46·16	9·9302	51·25
11·720	59·09	12·191	64·40	15·956	43·17	12·323	49·21

and thermodynamic dissociation constants have been calculated as described above. In water, the values $K = 0{\cdot}0049$ for zinc sulphate and $K = 0{\cdot}0043$ for copper sulphate given by Owen and Gurry (*loc. cit.*) have been adopted. Values of pK ($= -\log K$) (cf. Table III) have been plotted against $1/D$ in Figs. 1, 2, and 3; in each case the variation is linear, within the limits of experimental error, over the range studied.

FIG. 2.

Variation of dissociation constant with dielectric constant for zinc sulphate in mixed solvents.

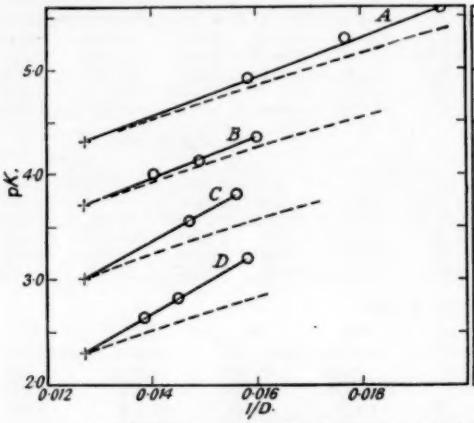
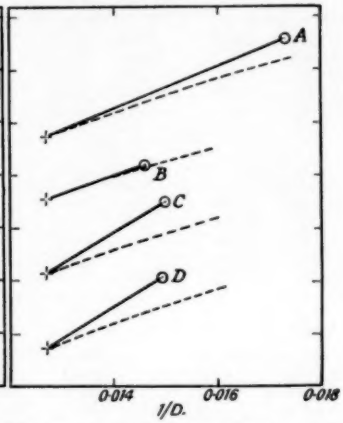


FIG. 3.

Variation of dissociation constant with dielectric constant for copper sulphate in mixed solvents.



A, Dioxan–water. B, Glycol–water. C, Ethanol–water. D, Acetone–water.

Results for ethanol–, glycol–, and dioxan–water mixtures have been displaced vertically by 0·7, 1·4 and 2 pK units respectively, for clarity.

TABLE III.

Dissociation constants in mixed solvents.

Solvent.	Run.	D.	Λ_0.	$10^2\eta$.	$\Lambda_0\eta$.	10^5K.	Solvent.	Run.	D.	Λ_0.	$10^2\eta$.	$\Lambda_0\eta$.	10^5K.
		Zinc malonate.							*Zinc sulphate.*				
Dioxan–water	1	69·40	95·0	10·42	0·990	7·19	Dioxan–water	15	63·20	99·1	12·40	1·229	120·6
	2	67·60	88·0	11·40	1·003	5·61		16	56·00	88·2	14·10	1·244	48·5
	3	63·40	86·0	12·35	1·062	3·13		17	51·20	77·2	15·25	1·177	25·8
	4	61·60	84·5	12·75	1·077	2·39	Acetone–water	18	72·40	108·0	11·17	1·206	222·0
	5	59·60	83·0	13·43	1·015	1·70		19	68·90	97·2	12·17	1·183	152·0
Acetone–water	6	71·90	89·0	11·33	1·008	6·36		20	61·60	86·3	12·75	1·100	63·4
	7	70·40	86·0	11·80	1·015	4·77	Glycol–water	21	70·65	72·0	17·50	1·260	251·0
	8	67·10	80·0	12·60	1·008	2·70		22	66·90	52·7	24·00	1·265	184·0
Glycol–water	9	73·20	79·0	14·00	1·106	8·44		23	62·20	36·7	35·00	1·284	110·0
	10	70·85	63·0	17·20	1·084	6·40	Ethanol–water	24	68·20	77·3	17·05	1·318	138·4
	11	68·75	51·5	20·50	1·056	4·91		25	64·10	67·6	19·75	1·335	76·6
	12	66·72	42·0	24·50	1·029	3·78							
Ethanol–water	13	70·70	70·0	15·10	1·057	5·81							
	14	66·80	50·0	18·10	0·905	3·97							
									Copper sulphate.				
Dioxan–water	26	57·80	95·0	13·67	1·299	49·4	Glycol–water	28	68·20	57·8	21·50	1·243	208·0
Acetone–water	27	66·90	93·0	12·65	1·176	90·5	Ethanol–water	29	66·40	71·0	18·10	1·285	89·7

Although, on the basis of a simple electrostatic treatment association should increase regularly with decreasing dielectric constant, in a number of systems it appears that marked specific interaction effects occur. Thus Burgess and Kraus (*J. Amer. Chem. Soc.*, 1948, **70**, 706)

have shown that the addition of relatively small amounts of water to solutions of metal picrates in pyridine causes abrupt increases in K. Effects of this nature have been attributed to specific interaction between solute ions and added solvent molecules leading to changes in a, the apparent distance of closest approach for an ion pair. From the present results it appears, however, that no marked specific interaction effects occur in the water-rich binary mixtures studied. The approximate constancy of the Walden–Stokes product $\Lambda_0\eta$ indicates that the effective radii of the free ions undergo no great change, and the similarity and regularity of the pK–$1/D$ curves indicate that decrease in dielectric constant is the main factor responsible for decrease in K.

If association is purely electrostatic to give ion pairs, then it is possible to predict the variation of K with D. On substituting the appropriate values for dissociation constants in water into the Bjerrum equation (*Kgl. Danske Vidensk. Selskab.*, 1926, **7**, No. 9), the values 2·14, 4·52, and 4·23 A. are obtained for the "a" parameters of zinc malonate, zinc sulphate, and copper sulphate respectively. Assuming these values to remain unchanged, the pK–$1/D$ curves shown as broken lines in Figs. 1, 2, and 3 have been calculated. In order to examine the extent to which the results were dependent on the nature of the extrapolation function used, values for Λ_0 and pK have also been derived using the extrapolation methods given by Fuoss and Kraus (*J. Amer. Chem. Soc.*, 1933, **55**, 476) and by Shedlovsky (*J. Franklin Inst.*, 1938, **225**, 739). The values obtained for a typical series of results are compared in Table IV. It appears that, whilst the values found for K depend to some extent on the manner in which $\alpha\Lambda$ is assumed to approach the limiting law, the magnitude of such dependence is small.

TABLE IV.

Zinc sulphate in 18·01% *w/w ethanol solutions* (*run* 24).

Extrapolation method.	Λ_0.	pK.
Davies	77·3	2·859
Shedlovsky	77·5	2·921
Fuoss and Kraus	77·5	2·887

The pK–$1/D$ curves for zinc sulphate and copper sulphate are almost coincident and are slightly less steep than the corresponding curves for zinc malonate. With both zinc sulphate and copper sulphate the increase in pK with decrease in D is somewhat greater than predicted; the reason for this is not clear, although it is of interest that measurements on lanthanum ferricyanide solutions in mixed solvents (James, *loc. cit.*) show similar but smaller deviations. It may be that errors are introduced by the use of the solvent dielectric constant in the Bjerrum equation when the value for "a" is small, as it appears that at distances of less than about 4 A. from an ion the dielectric constant is a rapidly varying quantity (Collie, Hasted, and Ritson, *J. Chem. Physics*, 1948, **16**, 1).

With zinc malonate, deviations from the theoretical Bjerrum curve are in the opposite sense, the observed decrease in K with decrease in D being less than calculated. Few measurements for other salts are available for comparison, although similar behaviour has been observed with the abnormally weak salt, lead chloride, and with organic acids in mixed solvents (James, *loc. cit.*). It is possible that such behaviour is characteristic and that dissociation constants are less dependent on dielectric constant when association is not determined purely by Coulomb forces. Ives (*J.*, 1933, 1360) and Jones, Monk, and Davies (*J.*, 1949, 2693) have pointed out that, in a given solvent, dissociation constants depend mainly on two factors, the solvation energies and the energy of interaction of the ions. With weak salts such as zinc malonate, the energy of interaction prevails, and no solvent molecules can intervene between anion and cation. With salts such as zinc sulphate, copper sulphate, and lanthanum ferricyanide, the interaction energy is much less, and ion pairs are formed between solvated ions.

The author thanks Dr. J. C. Speakman for many valuable discussions.

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33. *The Phosphorus Metabolism of* Bact. lactis aerogenes.

By P. C. Caldwell and Sir Cyril Hinshelwood.

A survey has been made of certain aspects of the phosphorus metabolism of the coliform organism *Bact. lactis aerogenes*. The cells are found to have a constant phosphorus requirement during the period of logarithmic growth, but under adverse conditions division can continue without further uptake of phosphorus from the medium.

No significant lowering of the growth rate can be detected at phosphate concentrations as low as 10^{-6} M.

In glucose media, buffered with veronal, phosphorylated intermediates, which probably contain a ribose-3 phosphate linkage, are built up inside the cells during the lag phase, reach a steady level during the logarithmic period, and decline towards the onset of the stationary phase. Intermediates of this type are not, however, detected during growth in glycerol–veronal media. The bearing of the results on the question of nucleic acid synthesis is discussed.

The cells utilise free inorganic phosphate to the exclusion of the nucleotide guanylic acid supplied in the medium—as shown by experiments with ^{32}P.

The work described in this paper forms part of a general study of the phosphorus metabolism of *Bact. lactis aerogenes*. Phosphorus, which is normally supplied in the synthetic culture medium as inorganic phosphate, is required for the production of a variety of substances. Some of these are involved in intermediary metabolism whereas others form an integral part of the cell structure.

The first problem to be dealt with is the relationship between the assimilation of phosphorus from the culture medium and the growth of the organism. Next the influence of the phosphate-ion concentration on the rate of growth is discussed, and it is shown that, even at the lowest concentrations accessible to experiment, the uptake of phosphorus has not yet become a rate-controlling step. The variations in the phosphorus content of the cells during the growth cycle are then considered, and alterations in the amount of various phosphorylated intermediates are described. In certain circumstances, these appear to be formed more rapidly than they are removed, and they show systematic rises and falls during the growth cycle. Finally, since substances of the nucleotide type must constitute necessary intermediates, the effect of guanylic acid on the growth of the cells is investigated.

Assimilation of Phosphorus from the Culture Medium.—The usual culture medium contains glucose (or some alternative carbon source), ammonium sulphate, magnesium sulphate, and a mixture of alkaline phosphates which serves both as a supply of phosphorus and as a buffer. Since the concentrations of phosphate required for adequate buffering are much greater than the amounts assimilated by the cells, chemical estimation of the removal of phosphorus from the normal culture medium is not practicable. It was necessary, therefore, to provide an alternative buffer, and veronal (sodium diethylbarbiturate) was used for this purpose. It interferes to some extent with growth, which is a disadvantage, but after a number of subcultures the cells show partial adaptation (though the mean generation time never drops to the value found in the normal culture medium).

Measurements of phosphorus uptake during the logarithmic phase show that the amount assimilated at any time is given by the relation:

$dx/dt = kx$, where x is the amount of phosphorus assimilated and k the growth rate constant.

This is of the same form as the equation which governs the increase in the number of cells:

$dn/dt = kn$, where n is the number of cells.

A plot of log x against time is linear, and a typical example is shown in Fig. 1, where it is compared with the corresponding growth curve.

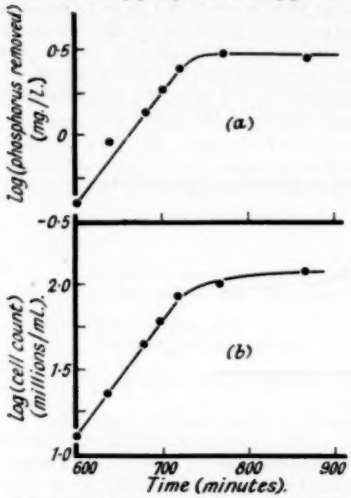
The fact that the assimilation is represented by an equation, identical in form with that for the multiplication of the cells, suggests that during the logarithmic period the requirement for phosphorus is steady. (This conclusion is not, however, valid for the lag and the stationary phase, as will appear.)

The relative amounts of phosphorus and nitrogen in cells can be found if the nitrogen content of a culture is compared with the quantity of phosphorus which it has assimilated. The ratio

phosphorus/nitrogen is found to be 0·29 for cells growing in the presence of veronal. This compares with the value of 0·20 found by Taylor (*J. Biol. Chem.*, 1946, **165**, 271) from analysis of the material of *Bact. coli* grown in a synthetic medium.

FIG. 1.

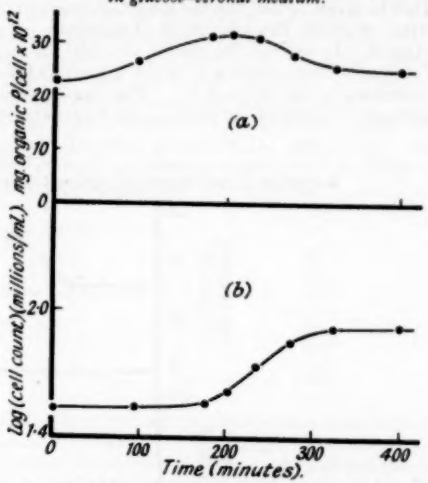
Assimilation of phosphorus during growth.



(*a*) *Removal of phosphorus from medium.* (*b*) *Growth curve. Initial phosphate concentration, 25 mg./l.*

FIG. 2.

Variation of total organic phosphorus during growth in glucose–veronal medium.



(*a*) *Variation of phosphorus per cell.* (*b*) *Growth curve. The two time scales are identical.*

This figure is constructed by the superposition of two sets of experimental results—one set taken to the end of lag, the other carried into the stationary phase.

The results of these experiments are summarised in Table I where values of the mean generation time obtained from the rate of assimilation of phosphorus are compared with those obtained from the rate of increase of cell numbers (mean generation time = $k/\ln 2$).

TABLE I.

Initial phosphate concn., mg./l.	Mean generation time (min.). From cell count.	From phosphorus assimilated.	Initial phosphate concn., mg./l.	Mean generation time (min.). From cell count.	From phosphorus assimilated.
50	60	60	10	70	60
25	45	48	5	62	55
20	48	52	1	72	—
15	50	45	0·1	75	—

Phosphate-ion Concentration and Growth Rate.—Table I shows that, within the range of conditions studied, very little, if any, systematic variation in growth rate can be detected over a 500-fold range of concentration, the mean generation time showing only slight increases of doubtful significance at phosphorus concentrations as low as 10^{-6}M. Chemical estimation shows that the inorganic phosphate in the medium must become almost completely exhausted before any serious effect is observed. The rate of growth cannot be measured in the normal way at phosphate concentrations below 10^{-6}M. because the cell numbers involved are too small, but it is very likely that a decrease would eventually be found. This investigation merely sets a limit above which no important fall occurs.

A somewhat different state of affairs is encountered if the concentration of the carbohydrate component of the medium is lowered. Various investigators, in particular Monod ("La Croissance des Cultures Bactériennes," Paris, 1942), have shown that considerable decreases in the rate of growth occur when the carbohydrate concentration is reduced to about 10^{-6}M.

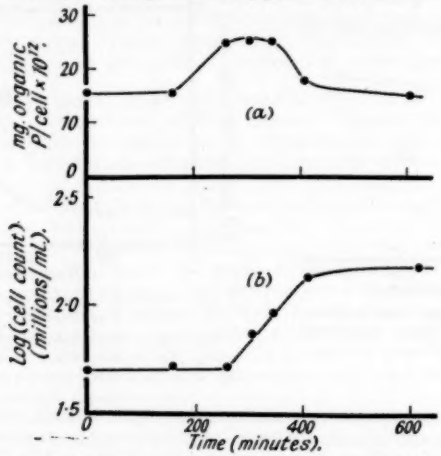
In most reactions involving enzymes, the dependence of the rate, r, on the substrate concentration, c, can be expressed by an equation of the form :

$$r = k_\infty c/(c + K_m)$$

where k_∞ is the limiting rate which is attained at high substrate concentrations and K_m is the concentration at which the rate is half the maximum value. This relation can be interpreted either in terms of an enzyme-substrate complex (Michaelis–Menten equation) or in terms of a surface reaction, the adsorption of molecules on the enzyme being governed by the Langmuir isotherm. In general, the growth constant for the cells, k, will be proportional to r. The region of substrate concentration at which a marked lowering of the rate of growth takes place will be determined by the value of K_m. The magnitude of this depends on the tightness with which the substrate is bound to the enzyme, the larger the value the looser being the binding.

FIG. 3.

Variation of total organic phosphorus during growth in glycerol–veronal medium.



(*a*) *Variation of phosphorus per cell.* (*b*) *Growth curve. The two time scales are identical.*

The experimental results suggest that the value of K_m governing the processes responsible for the assimilation of carbohydrates must be considerably larger than that for the process involved in the uptake of phosphate. This means that the binding of phosphate ions to the relevant enzymes must be tighter than that of carbohydrates, as is quite understandable, since with phosphate an electrostatic interaction is superimposed on the van der Waals binding. With carbohydrate molecules there is no ionic interaction, and they are less tightly held. It is of interest that Lewis and Hinshelwood (*J.*, 1948, 841) were unable to detect any decrease in the rate of growth when the concentration of ammonium ions in the medium was reduced, which indicates that these, like phosphate, are more firmly bound than carbohydrate molecules as a result of an ionic interaction.

Variations in the Cell Phosphorus during the Growth Cycle.—Fig. 2 shows the variations in the total organic phosphorus per cell during growth in the glucose–veronal medium. During the lag period the amount rises and reaches a steady value at the beginning of the logarithmic-growth phase. As the stationary phase is approached it declines to its original level. Fig. 3 shows that the same sequence of events takes place in a veronal medium in which the glucose is replaced by glycerol, and a similar state of affairs is observed under anaërobic conditions in a glucose–veronal and in a (−)-D-arabinose–veronal medium.

In these particular examples the primary factor which limits growth is the exhaustion of the phosphate provided in the medium. The effects observed in media where the breakdown of the buffer is the limiting factor are, however, similar.

The deoxyribose nucleic acid content per cell of *Bact. lactis aerogenes* has been shown to be

approximately constant, even under conditions of phosphorus deficiency (*J.*, 1950, 1415). Changes in the amount of total organic phosphorus per cell during the growth cycle should represent, therefore, variations in the remainder of the cell phosphorus relative to the deoxyribose nucleic acid. In the lag phase, the total phosphorus in the cell increases at the expense of the phosphate in the medium. At the end of the growth phase, on the other hand, a certain amount of cell division takes place after the conversion of phosphate into the organic form has virtually ceased, the cells becoming smaller in the process. Since an increase in the number of cells must, by the previous result, involve an increase in the deoxyribose nucleic acid in the culture as a whole, the synthesis of this can presumably occur at the expense of the other organic phosphates. (This explains the observation that the total population supported by a medium does not fall off linearly as the inorganic phosphate concentration drops towards zero.)

Estimations have been carried out of the amounts of ribose and deoxyribose nucleic acid in cells growing in a variety of media and have been reported previously (*J.*, 1950, 1415). The determinations on cells growing in the glucose–veronal medium are summarised in Table II, which gives the percentage of the total phosphorus present in the various forms.

TABLE II.

	%
Deoxyribose nucleic acid	18·1
Ribose nucleic acid (including free pentose nucleotides)	61·3
Total nucleic acid	79·4
Other organic phosphorus	20·6
Total organic phosphorus	100·0

This shows that most of the cell phosphorus, other than deoxyribose nucleic acid, is in the form either of ribose nucleic acid or free pentose nucleotides. The changes in the amount of organic phosphorus per cell may, therefore, be due to variations in this group of substances, and it is these which are probably converted into deoxyribose nucleic acid at the end of logarithmic growth.

These observations bear some relation to those of Malmgren and Hyden (*Acta Path. Microbiol. Scand.*, 1947, **24**, 448). These authors have studied the ultra-violet absorption of a number of bacterial species during the growth cycle in broth. Their results show that, in *Bact. lactis aerogenes* and other Gram-negative organisms, substances showing the absorption of nucleic acids are built up in the cells during the lag and reach a maximum just before the onset of active growth, after which they decline. Although these experiments were carried out with a different medium, a comparison with those reported here is probably legitimate. There is a difference in that the absorption measurements show a maximum to be reached at the end of the lag, whereas the present work shows certain substances to rise in amount during the lag to a value which is maintained during much of the logarithmic phase. The ultra-violet absorption is not, however, specific for the nucleic acids themselves, but may include contributions from free purines, nucleosides, and nucleotides. The two sets of observations become compatible if part of the increase in absorption which is observed during the lag is attributed to an accumulation of free purines and nucleosides. Towards the end of the lag, conversion of these into nucleotides and nucleic acid takes place, the phosphorus content of the cells increases, and, when this has reached an optimum level, growth begins. At this stage the rate of removal of free purines and pyrimidines becomes equal to their rate of formation and, as the cells divide, their total purine content (and hence the intensity of their absorption in the ultra-violet) decreases.

The Later Stages of Phosphorus Metabolism.—The foregoing discussion has raised the question of the occurrence of metabolic intermediates in the cell. Between the assimilation of inorganic phosphate and the final steps leading to the formation of nucleic acid there exists an intricate series of reactions. The progress of most of these cannot, at the moment, be demonstrated experimentally, but it has proved possible, under certain conditions, to detect the formation and disappearance of substances which may be the immediate precursors of the polymerised nucleic acids.

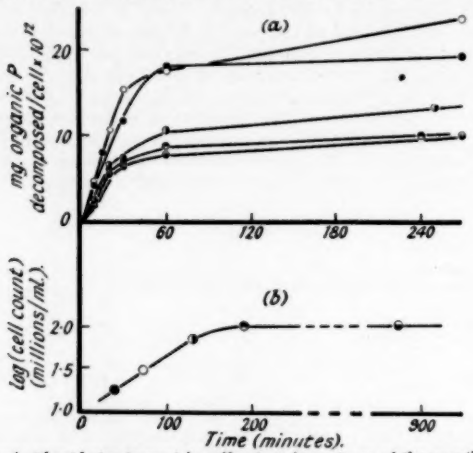
Some differentiation of the various types of organic phosphate present in the cells can be made by examination of the rates of hydrolysis of the ester linkages by N-sulphuric acid at 100°. Under these conditions the organisms are lysed in a few minutes and their contents dispersed into solution where they become exposed to the action of the acid.

Fig. 4 shows, for cultures at various stages of growth in the glucose–veronal medium, the

amounts of inorganic phosphate formed per cell after different periods of heating. The marking of the curves in the upper part of the diagram corresponds to that in the lower part which shows the stage of the growth cycle at which the cultures were sampled. The form of the curves shows

FIG. 4.

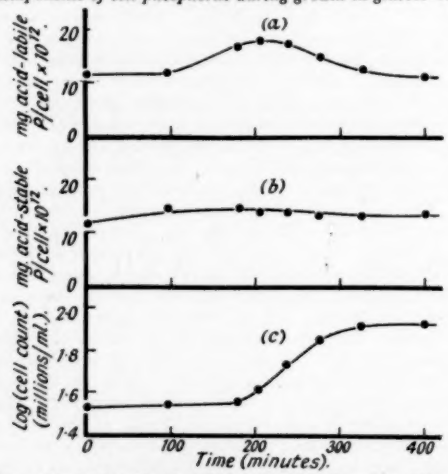
Hydrolysis of organic phosphates in the cell by N*-sulphuric acid at* 100°.



(a) *Hydrolysis of organic phosphates present in cells at various stages of the growth cycle.* (b) *Composite growth curve in which the marking of the points corresponds to the separate curves in* (a).

FIG. 5.

Variation of components of cell phosphorus during growth in glucose–veronal medium.



(a) *Acid-labile phosphate.* (b) *Acid-stable phosphate.* (c) *Growth curve. The time scales are identical.*

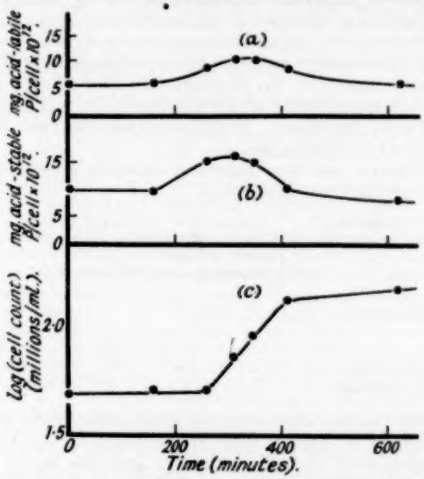
that one part of the organic phosphate in the cells is completely decomposed after 60 minutes. This acid-labile fraction probably consists of ribose-3 phosphate, adenosine-3 phosphate, and guanosine-3 phosphate (see following paper), and it will be seen that a considerably larger quantity of it is present during the logarithmic period than is present in the stationary phase. A

reasonably good estimate of the amounts of phosphorus in the acid-labile and acid-stable fractions, respectively, is obtainable from the proportion of the total hydrolysis which takes place in 60 minutes.

Fig. 5 shows results obtained for growth in a glucose–veronal medium. The relative amounts per cell of these two fractions are plotted against time, the corresponding growth curve being shown for comparison. During the lag, ribose-3 phosphate and purine nucleotides containing a ribose-3 phosphate linkage are built up to a steady level which is attained just before the beginning of active growth. They remain at this higher level during much of the logarithmic period, and show a sharp decline at the approach of the stationary phase. The acid-stable group of phosphates on the other hand remains nearly constant. The rise in the labile group at the end of the lag takes place entirely at the expense of the inorganic phosphate in the medium.

FIG. 6.

Variation of the components of the cell phosphorus during growth in glycerol–veronal medium.



(*a*) *Acid-labile phosphate.* (*b*) *Acid-stable phosphate.* (*c*) *Growth curve. The time scales are identical.*

During the decline at the end of the logarithmic phase, however, little inorganic phosphate is converted into the organic form, and synthesis of the acid-stable group continues for a time largely at the expense of the labile group. This interconversion is reflected in the relative percentages of the total phosphorus corresponding to the two groups in the logarithmic phase and in the stationary phase, respectively. The figures in Table III are typical.

TABLE III.

	Early logarithmic phase.	Late logarithmic phase.	Early stationary phase.	Late stationary phase.
% of total P present as the labile group	56	53	45	47
% of total P present as the stable group	44	47	55	53

These changes are also observed in growth under anaërobic conditions in the glucose–veronal medium. In the medium containing glycerol as carbon source, however, the unstable intermediates which are convertible into other substances under unfavourable conditions of growth do not appear. The sequence of events in this medium is represented in Fig. 6 which shows that both groups of phosphate increase during the lag, reach a ma..imum value during the logarithmic period, and decline to a comparable extent in the stationary phase. That no large interconversion of the two groups occurs at the end of growth is shown by the values given in Table IV.

TABLE IV.

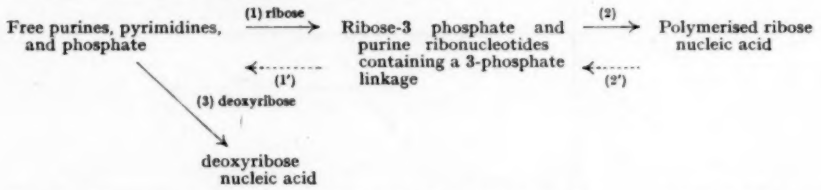
	Early logarithmic phase.	Late logarithmic phase.	Early stationary phase.	Late stationary phase.
% of total P present as the labile group	41	43	43	40
% of total P present as the stable group	59	57	57	60

The fact that labile intermediates cannot be detected during growth in glycerol suggests that in this medium they may be formed with greater difficulty and therefore consumed as rapidly as they are formed.

These experiments show that, in conditions of phosphorus shortage in the glucose–veronal medium, part of that needed for the synthesis of deoxyribose nucleic acid may be derived from free ribose nucleotides. In similar circumstances in glycerol, however, this synthesis must presumably take place at the expense of a breakdown of ribose nucleic acid itself.

The formation of ribose-3 phosphate intermediates during growth in the glucose–veronal medium may to some extent be an accident of the conditions of growth. Veronal, as mentioned earlier, is an inhibitor. Barbiturates are known to inhibit the metabolism of uracil which suggests that they act by blocking the enzymes responsible for the utilisation of this substance. Since these enzymes may well be instrumental in the production of uridylic acid from uracil and ribose-3 phosphate, interference with their normal action may lead to an accumulation of the latter which would not occur under normal conditions. Whether any accumulation takes place in the normal glucose culture medium is as yet uncertain.

The observations which have just been discussed suggest as possible the following scheme for the events leading to the synthesis of nucleic acid.



The dotted arrows indicate the probable route by which deoxyribose nucleic acid is formed at the expense of ribose nucleic acid, since a direct interconversion is highly unlikely. In general, the process (1) will be associated with the transition from the lag to the logarithmic period, processes (2) and (3) with logarithmic growth, and the processes (1') and (2') come into operation to feed (3) at the end of growth.

Utilisation of Inorganic Phosphate by the Cells in Preference to Guanylic Acid (work carried out in collaboration with Dr. C. J. Danby).—Purine nucleotides are probably intermediates in the formation of nucleic acid, and it is of interest to discover whether these substances are assimilated in preference to inorganic phosphate when they are provided in the culture medium. For this purpose two cultures were grown in glucose–veronal media containing enough radioactive inorganic phosphate to cover the requirements of the cells. To one was added also a quantity of inactive guanosine-3 phosphate (guanylic acid) equivalent in phosphorus content to the active inorganic phosphate.

TABLE V.

Culture with guanylic acid.		Control.	
Number of cells (10^6/ml.).	Activity (Counts/mg. cell-N).	Number of cells (10^6/ml.).	Activity (Counts/mg. cell-N).
82	447	64	444
273	433	181	436
435	371	441	395

If the guanylic acid were taken up preferentially, the activity, per unit amount of nitrogen, of cells growing in its presence, should be lower than that of the cells in the control experiment. Table V shows that the activities are the same for both cultures, and thus indicates that none of the cell phosphorus is derived from guanylic acid.

Evidently the bacteria prefer to synthesise nucleotides in their own way or are, perhaps, compelled to do so if for some reason guanylic acid is unable to penetrate the cell wall.

Experimental.

Growth Media.—The media used had the composition: carbon source (glucose 50 g./l.; glycerol, (−)-D-arabinose 10 g./l.), 100 ml.; veronal buffer (sodium diethylbarbiturate 9·3 g./l.; pH 7·25), 100 ml.; sodium and potassium phosphates (180 mg. of phosphate per l.), x ml.; sterile water, $(100 - x)$ ml.; ammonium sulphate (5 g./l.), 50 ml.; magnesium sulphate (1 g./l.), 10 ml. (The relative amounts of phosphate and distilled water depended on the concentration required in the final medium.) The mean generation time in the veronal medium is usually about 60 minutes.

Growth of Cultures.—All the experiments were carried out on cultures growing at 40·0° in sterile cylinders. Losses of liquid by evaporation from aerated cultures were corrected when necessary.

Measurement of Cell Numbers and Cell Nitrogen.—For this purpose a 2-ml. sample of the culture was taken and treated with 1 drop of 40% formalin, the number of cells being determined by hæmocytometer. The amount of cell nitrogen was measured turbidimetrically (*J.*, 1950, 1415).

Measurement of Inorganic Phosphorus.—Two methods were employed, the Fiske–Subbarow method (*J. Biol Chem.*, 1925, **66**, 375) and the Berenblum–Chain method (*Biochem. J.*, 1938, **32**, 295). In the former, a period of 60 minutes was allowed to elapse between the addition of the reagents and determination of the colour intensity, but otherwise the method was used in its original form. A number of modifications were, however, introduced into the latter, which was carried out as follows. The reagents employed were: stock stannous chloride solution, 10 g. of the salt in 25 ml. of concentrated hydrochloric acid; stannous chloride solution for reduction, 0·5 ml. of the stock solution in 5 ml. of N-hydrochloric acid; approximately N-hydrochloric acid; 11N-sulphuric acid; ammonium molybdate solution, 10 g. of the salt in 100 ml. of distilled water; *iso*butanol.

Quantities of the diluted stannous chloride reagent, N-hydrochloric acid, and ammonium molybdate solution were cooled to 0° and saturated with *iso*butanol. A quantity of *iso*butanol was also cooled to 0° and saturated with water. 10 Ml. of the solution under examination were treated with 1 ml. of 11N-sulphuric acid and then cooled to 0°. 2 Ml. of *iso*butanol were added, and the aqueous layer was saturated with this by shaking. 10 Ml. of the saturated layer were placed in a separating funnel, 1 ml. of the ammonium molybdate solution and 5 ml. of the *iso*butanol were added, and the contents of the funnel were shaken for 60 seconds, after which the aqueous layer was run off. The *iso*butanol layer, into which all the phosphomolybdate had passed, was washed twice with the N-hydrochloric acid, and the *iso*butanol layer was then treated with 5 ml. of the reducing solution whereupon the molybdenum-blue colour was formed. A sample of this layer was transferred to the absorptiometer cell and allowed to reach room temperature; the colour intensity was then compared with a standard.

The main differences between this procedure and that suggested by Berenblum and Chain are the following: (1) The reducing solution is made up in hydrochloric acid instead of sulphuric acid, since a solution of stannous chloride in the former was found to keep its activity for a longer period. (2) All the solutions are saturated with *iso*butanol, and the *iso*butanol with water. This eliminates any significant changes in the volume of the *iso*butanol layer during the measurements, and obviates the necessity for dilution to a standard volume before the colour intensity is measured. Furthermore, it eliminates errors due to possible loss of part of the *iso*butanol layer when one of the aqueous layers is removed. (3) By operation at 0° a rise to room temperature is provided for, and this removes water droplets in the *iso*butanol layer which would otherwise interfere with the estimation of the colour intensity. The need for adding ethyl alcohol with its attendant complications is thereby avoided.

Experiments on the Assimilation of Inorganic Phosphate.—At intervals during growth two samples were taken, the first for determination of the mean generation time from the hæmocytometer count, the second for phosphate determination. If the concentration of phosphate lay between 50 mg./l. and 10 mg./l., 25 ml. were taken and treated with 5 ml. of 10% trichloroacetic acid. The cells were removed by centrifugation, and the free inorganic phosphate in 25 ml. of the supernatant liquid was determined by the Fiske–Subbarow method. If the concentration was below 10 mg./l., a 10-ml. sample was taken, treated with 2 ml. of 10% trichloroacetic acid and centrifuged, the phosphate determination being carried out on 10 ml. of the supernatant liquid by the modified Berenblum–Chain method. (At very low concentrations a 25-ml. sample was used for this determination.)

The Effect of Phosphate-ion Concentration on Growth Rate.—The relevant results were obtained mainly from the experiments described above. All the mean generation times were derived from the measurement of cell numbers with a hæmocytometer.

Experiments on the Variations in the Organic-Phosphorus Content of the Cells during the Growth Cycle.—Samples were removed from the culture at intervals, one of 2 ml. for measurement of the cell number, the other of 10 ml. being treated with 1 ml. of sulphuric acid (to stop gro th) and centrifuged. 10 Ml. of the supernatant liquid were then analysed by the Berenblum–Chain method. Since, as other experiments (cf. following paper) have shown that nearly all the organic phosphate in a culture is located inside the cells, the amount of inorganic phosphate which has disappeared after a given time may be taken as equivalent to their organic-phosphorus content.

Experiments on the Occurrence of Phosphorylated Metabolic Intermediates in the Cells.—The first series of experiments under this heading involved a determination under standard conditions of the rate of hydrolysis of the phosphate esters contained in the cells. A culture was inoculated, and at the appropriate stage of growth 250 ml. were centrifuged, the cells being then suspended in distilled water to a total volume of 250 ml. 10-Ml. samples were pipetted into glass tubes and treated with 1 ml. of 11N sulphuric acid. The tubes were sealed and heated for varying times at 100° after which the inorganic phosphate was determined in 10 ml. of the sample by the Berenblum–Chain method. The cells disintegrated after about 5 minutes, so that their structure had little effect on the rate of hydrolysis of the esters. In samples which had been heated for less than 10 minutes, however, sufficient cell debris remained to

interfere with the separation of the *iso*butanol layer from the aqueous layer in the phosphate analysis, and it was necessary to centrifuge these before the determination. The counts of the suspensions were also measured.

The second series of experiments was made as follows. Three samples were withdrawn from a culture at intervals. The first of these (2 ml.) was used for the measurement of cell numbers. The other two were both of 10 ml., and 1 ml. of 11N-sulphuric acid was added to each. One was centrifuged immediately and the total organic phosphate in the culture at the time of sampling was determined from the difference between the free inorganic phosphate remaining and that initially present. The second was placed in a sealed tube which was heated for 60 minutes at 100°, after which the inorganic phosphate was determined by the Berenblum–Chain method. Hence it was possible to find the amounts of " acid-labile " and " acid-stable " phosphate in the cells.

Experiments on the Ability of the Cells to use Guanylic Acid as a Source of Phosphorus.—These experiments were carried out with the collaboration of Dr. Danby whose counting equipment was used in measurements of the activities of the cells.

At stages during the growth of the two cultures a 2-ml. sample, for a determination of nitrogen content and a 10-ml. sample, for the measurement of the activity of the cells, were taken simultaneously. The latter was centrifuged and the cells were transferred to an aluminium disc. After they had been dried their activity was measured.

We should like to express thanks to the Department of Scientific and Industrial Research for the financial assistance which has rendered this work possible.

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34. *The Nature of the Phosphorus Compounds Present in Cells of* Bact. lactis aerogenes.

By P. C. CALDWELL.

The rate of hydrolysis by N-sulphuric acid at 100° of the phosphate ester linkages in cells of *Bact. lactis aerogenes* has been investigated. Three distinct stages in the reaction can be detected and it has proved possible to analyse the curves obtained into three separate first-order components. The first-order constants obtained are compared with those found for the breakdown of relevant model substances. The results suggest that the first two stages represent the hydrolysis of different linkages present in the nucleic acids and that the third represents the breakdown of phospholipoid. There is an indication that the nucleic acid in cells which have been subjected to phosphorus starvation may contain phosphate linkages not present in the nucleic acids derived from yeast and thymus.

VARIOUS results are available to give an overall picture of the distribution of phosphorus in the different forms in which it occurs in the bacterial cell (preceding paper; Taylor, *J. Biol. Chem.*, **1946, 165**, 271). About 80—90% of the phosphorus appears to be in the form of the nucleic acids and their simple components, while the remainder probably consists of phospholipoid. Furthermore, of the nucleic acid fraction, about 20% can be accounted for as deoxyribose nucleic acid and about 60% as ribose nucleic acid and ribose nucleotides.

To attempt any further subdivision of the cell phosphorus is difficult. Large quantities of culture must be grown to make identification of the phosphorus compounds by normal chemical methods practicable. It was shown in the previous paper, however, that a crude distinction could be detected in the cell phosphorus in so far as it was possible to distinguish two components which differed in the rate of hydrolysis of their phosphate ester linkages under the action of N-sulphuric acid at 100°. In the present paper the rate of hydrolysis of the different phosphate ester linkages in the cells has been examined in greater detail, and an attempt made to carry out a kinetic analysis. The rates observed with the cell components have been compared with those of deoxyribose and ribose nucleic acids and with those of simple ribose nucleotides.

The Rate of Hydrolysis of the Phosphate Ester Linkages in the Cells.—In these experiments a complete survey was made of the organic phosphates present in both the cells and the medium in which they were growing at the time of sampling. Only traces of organic phosphorus could be detected in the latter, and this appeared to consist chiefly of substances which were decomposed by N-sulphuric acid after 60 minutes at 100°. Of the phosphorus in the cells

themselves, about 10% was found to be in the form of adsorbed inorganic phosphate which could be removed by the action of acid at room temperature, whereas the remainder was in organic form.

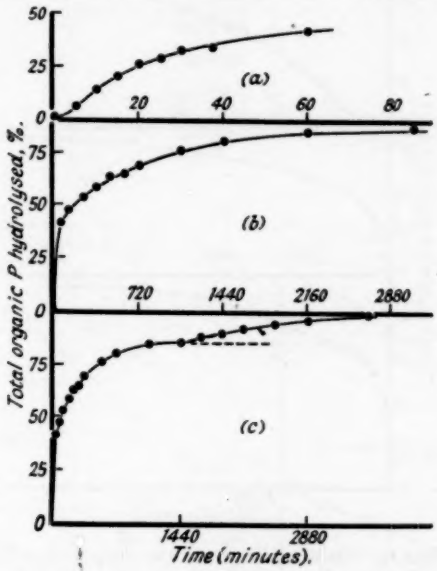
Fig. 1 shows the percentage of this organic phosphorus which had undergone decomposition after varying times in N-sulphuric acid at 100°, for cells which were sampled during the logarithmic-growth phase. Fig. 2 shows the same for cells which were sampled after a period of phosphorus starvation.

These two curves show that the organic phosphorus in the cells can be divided into three well-defined groups :

(1) a fraction which is completely decomposed after 60 minutes,
(2) a fraction which is decomposed after about 24—36 hours, and
(3) a fraction which is still not completely decomposed after 5 days.

FIG. 1.

Hydrolysis of organic phosphates present in actively growing cells (by N-sulphuric acid at 100°).



In the third of these groups the curves reveal a delay before decomposition sets in at all. This effect has been studied closely and appears to be reproducible. The possible reasons for it will be discussed later.

The decomposition of phosphate ester in the presence of hydrogen ions usually shows first-order kinetics provided that the phosphoric acid formed is not sufficient materially to alter the pH. An attempt has been made, therefore, to analyse the three stages, in which the cell phosphorus decomposes, into three first-order reactions. Though this analysis is complicated by the fact that the third component shows the delayed hydrolysis, a visual inspection of the curves in Figures 1 and 2 will show that the second stage is almost completed before the third stage has begun. The end-point for the second stage can thus be obtained by inspection.

In a first-order reaction log (residual reactant), *i.e.*, log $(a - x)$, is a linear function of time. Fig. 3*a* shows the first-order plot for the third stage of the curve shown in Fig. 1. The end-point was known from the total phosphorus of the cell. Fig. 3*b* shows a similar plot for the second stage of the curve shown in Fig. 1, the end-point being obtained by inspection. This plot shows an abrupt deviation from linearity between 60 minutes and zero time, since during this period the first stage of the hydrolysis is also taking place. The second stage can be separated from the first by the following procedure. The linear portion of the curve (*B* to *C*),

which relates solely to the second stage, is extrapolated to A to give the complete first-order plot for the second stage.

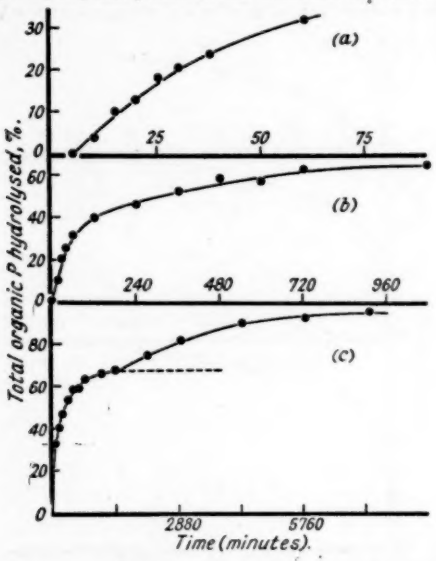
$(a_2 - x)$ for the second group in the range $t = 0$ to $t = 60$ minutes can be obtained from points on AB. If these values are subtracted from the total organic phosphorus, the values of $(a_1 - x)$, *i.e.*, organic phosphorus of the first group which remains undecomposed at these times, can be obtained. A plot of log $(a_1 - x)$ against t may now be made for the first stage and this is shown in Fig. 3*c*.

Figs. 4*a*, 4*b*, and 4*c* show the various components of the curve in Fig. 2 after a kinetic analysis carried out in a similar manner.

The velocity constants for the decomposition of the various components can be evaluated from the slope of the log $(a - x)/t$ curves, and the results are summarised in Table I.

FIG. 2.

Hydrolysis of organic phosphates present in cells which have been starved of phosphorus.



The numbers show that the rate of hydrolysis of the components in the first group remains unchanged on transition from the phase of active growth to conditions of phosphorus starvation. The velocity constants for the third stage also remain sensibly constant. In the second group, however, a remarkable change is observed, the velocity constant increasing by 100%, a change which is outside the limits of experimental error.

Before the velocity constants obtained for the breakdown of the phosphates present in the cells are compared with those obtained with model compounds, the approximate nature of such a comparison must be emphasised. Differentiation of two phosphorylated substances in a composite hydrolysis curve is only possible if their velocity constants are reasonably widely separated (numerical trials suggest by about 100%). It would be erroneous, therefore, to regard each stage in the hydrolysis curve found with the cells as arising necessarily from one single type of phosphate linkage. Within each of the three groups there are probably a number of different substances, with rates of hydrolysis close enough to give the impression of an approximately first-order reaction, the velocity constant for which represents some sort of average of those for the various components. (These considerations apply to the curves obtained with the nucleic acids, since these break down to give a variety of phosphorylated products.)

Comparison of the Rates of Hydrolysis of the Components of the Cell Phosphorus with those of the Nucleic Acids.—With a view to a possible identification of the components which contribute

TABLE I.

Velocity constants for the first-order hydrolysis of the phosphate ester linkages in cell suspensions in the nucleic acids and in various nucleotides.

	Cell suspensions		Nucleic acids	
	(1) cells actively growing.	(2) cells starved of phosphorus.	(1) yeast ribose nucleic acid.	(2) thymus deoxyribose nucleic acid.
The first stage :				
10^3k (min.$^{-1}$)	5·4	5·3	6·1	7·0
% of the total organic phosphorus	38	25; 32	52	30
The second stage :				
10^3k (min.$^{-1}$)	1·4	3·1; 2·9	0·81	1·7
% of the total organic phosphorus	47	42; 34	48	70
The third stage :				
10^4k (min.$^{-1}$)	4·0	3·3; 4·7		
% of the total organic phosphorus	15	33; 34		

	Nucleotides, etc.			
	(1) Guanosine-3 phosphate.	(2) Uridine-3 phosphate.	(3) Adenosine-5 phosphate.	(4) Lipoid extract of the cells.
k (min.$^{-1}$)	$7·0 \times 10^{-4}$	$0·47 \times 10^{-3}$	$2·7 \times 10^{-4}$	$2·4 \times 10^{-4}$

FIG. 3.

First-order plots for the various stages of the hydrolysis of phosphates present in actively growing cells.

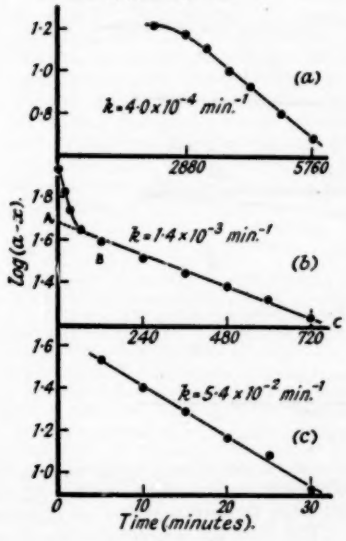
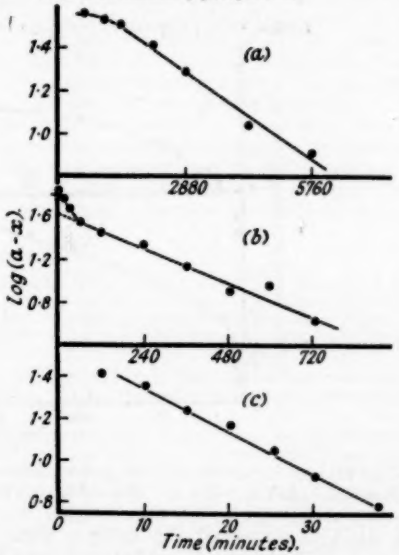


FIG. 4.

First-order plots for the various stages of the hydrolysis of phosphates present in cells which have been starved of phosphorus.



to the hydrolysis curves obtained with the cells, the hydrolysis of the phosphate ester linkages in ribose and deoxyribose nucleic acids have been studied. The results for ribose nucleic acid are shown in Fig. 5. This shows two distinct stages which are similar to the first two stages observed with the cells. A kinetic analysis, as described, into two first-order reactions has been carried out.

Fig. 6 shows the hydrolysis curve for deoxyribose nucleic acid, which also decomposes in two stages. This curve also has been analysed into two components. The similarity between these curves and those for the first two stages in the breakdown of the cell phosphates strongly suggests that these stages represent the breakdown of nucleic acid. This identification would not be inconsistent with the analytical figures given earlier, since the first two stages account for 66—85% of the cell phosphorus.

FIG. 5.

Hydrolysis of phosphate ester linkages in ribose nucleic acid from yeast.

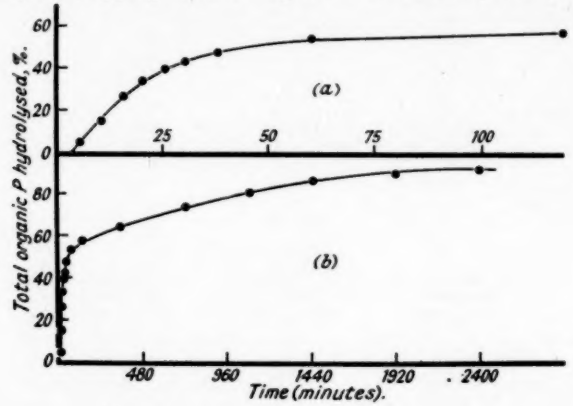
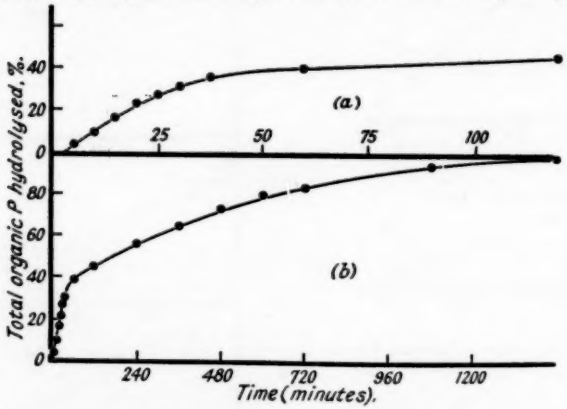


FIG. 6.

Hydrolysis of phosphate ester linkages in deoxyribose nucleic acid from thymus.



The velocity constants for the decomposition of the various components of the two nucleic acids are recorded in Table I. The values obtained for the first stage coincide within 10% and are in good agreement with those obtained for the first stage hydrolysis of the cell material. The values for the second stage differ by about 100%. The value for the second stage of the cells in logarithmic growth lies between those found for the two nucleic acids, and may arise from the combined hydrolysis of both types. On the other hand, the value for the second stage with cells which have been deprived of phosphorus is considerably higher than the values obtained with the two nucleic acids. This would suggest that in cells grown under these conditions the nucleic acid contains a phosphate ester linkage which is not found in the nucleic acids prepared from yeast and thymus.

The velocity constant for the third stage in the breakdown of the cell phosphates is considerably lower than that for any component of the nucleic acids, which suggests that this third group consists of something other than nucleic acid.

Comparison of the Rates of Hydrolysis of the Components of the Cell Phosphorus and of the Nucleic Acids with those of Certain Simple Nucleotides.—The hydrolysis of the following simple nucleotides has been studied: guanosine-3 phosphate, uridine-3 phosphate, and adenosine-5 phosphate. In N-sulphuric acid at 100° these all hydrolyse with first-order kinetics. The velocity constants obtained are summarised in Table I. This shows that the values for guanosine-3 phosphate (which is typical of ribose-3 phosphate and of purine nucleotides containing a ribose-3 phosphate linkage) and those for the first stage in the hydrolysis of both the cell phosphorus and the nucleic acids all fall within about 20% of one another. Thus the first stage appears to be due to the breakdown of purine nucleotides containing a 3-phosphate linkage. (This assumes that the kinetics of the hydrolysis of the deoxyribose nucleotides is similar to that of the ribose nucleotides.) The second stage in the breakdown of the cell phosphates and the nucleic acids may contain contributions from both pyrimidine nucleotide-3 phosphates and nucleotides (either purine or pyrimidine) containing other phosphate linkages.

It is not possible, however, to make a satisfactory identification of the components which contribute to this stage of the hydrolysis in either the cells or the nucleic acid since certain important model compounds (in particular, ribonucleotides containing a 2-phosphate linkage) are not available.

The value obtained with uridine-3 phosphate indicates that substances of this type may contribute to the second stage of the hydrolysis of yeast ribose nucleic acid. That obtained with adenosine-5 phosphate suggests that the nucleic acid present in cells which have been subjected to phosphorus starvation may possibly contain a 5-phosphate linkage.

The Nature of the Phosphorus Compounds which Contribute to the Third Stage of the Hydrolysis of the Cell Phosphates.—The proportion of the cell phosphorus present as phospholipoid was found to be about 8—9% of the total. Since the first two stages in the hydrolysis of the bacterial phosphorus, which account for between 70 and 85% of the total, can be attibuted to the breakdown of nucleic acid, it is likely that the third stage arises from the decomposition of phospholipoids. To test the correctness of this point of view the rate of hydrolysis of the organic phosphates from a chloroform extract of the cells was investigated. The reaction is of the first order, and the velocity constant is given in Table I. The value is somewhat lower than that found with the whole cells, but lies within the same range, and the assumption that the third stage arises from the breakdown of the phospholipoids seems probably correct.

No definite explanation can at present be offered for the fact that the third stage shows a delayed hydrolysis. None of the model compounds tried (including the lipoid extract) shows an induction period of this type. It may perhaps be assumed that the phospholipoid is dissolved in small globules of fat formed during the disintegration of the cells and that these must be destroyed by the acid before it can have any action on the phospholipoids themselves.

Experimental.

Experiments on the Decomposition of the Cell Phosphates.—The cells were grown in glucose–veronal media having the general composition described in the preceding paper. That used for the cells which were to be removed in the logarithmic phase contained 15 mg./l. of phosphate and that in which the cells were to be subjected to conditions of phosphorus starvation was buffered at an initial pH of 7·8 and contained 10 mg./l. of phosphate.

When the culture had reached the required phase of the growth cycle, 500 ml. of it were centrifuged. After removal of the supernatant liquid, which was kept for further examination, the cells were suspended in distilled water and diluted to a volume of 500 ml.

The rate of liberation of phosphoric acid from the phosphate esters in the cells was measured in the following way: 10-ml. samples of the cell suspension were pipetted into glass tubes and treated with 1 ml. of 11N-sulphuric acid. The tubes were then sealed and heated for varying times at 100°. The cells disintegrated after about 5 minutes and the various phosphate esters were dispersed into the solution.

After the heating, the tubes were opened and the inorganic phosphate formed was measured by the Berenblum–Chain method. In samples which had been heated for less than 5—10 minutes, sufficient cell debris remained to interfere with the separation of the *iso*butanol layer from the aqueous layer during the estimation, and this was therefore removed by centrifugation beforehand.

Determination of the total phosphorus in the suspensions was carried out after oxidation of the cell material with sulphuric acid.

The organic phosphates present in the supernatant liquids were investigated by the methods described above for the cell suspension.

Experiments on the Rates of Hydrolysis of the Phosphate Esters in the Nucleic Acids and their Derivatives.—The two nucleic acid samples and the guanosine-3 phosphate were purchased. The deoxyribose nucleic acid and the guanosine-3 phosphate were not subjected to any further purification. The ribose nucleic acid was purified by precipitation in mildly acid solution, after which it was centrifuged and washed with distilled water. It was slowly treated with sufficient alkali to bring the pH just to 7·0 and then reprecipitated as the sodium salt by the addition of alcohol. The samples of adenosine-5 phosphate and cytosine-3 phosphate had been prepared by synthetic methods.

Solutions which contained 40 mg./l. of each of these compounds were made in distilled water. The decomposition of the ester linkages by N-sulphuric acid at 100° was investigated by the method used for the examination of the cell suspensions.

Experiments on the Rate of Hydrolysis of the Phosphate Esters in a Lipoid Extract of the Cells.—A culture was grown in the normal glucose medium, and a quantity of this was centrifuged. The cells were subsequently suspended in isotonic saline and re-centrifuged. They were then dispersed in acetone and set aside for 24 hours. Extraction of the lipoid material was completed by addition to the suspension in acetone of an equal volume of chloroform and the heating of the mixture. The acetone and chloroform were then evaporated off, and the extracted fatty material was removed from the cell debris by partition between chloroform and water. The chloroform extract was emulsified in distilled water, and the chloroform itself removed by aeration to leave an aqueous emulsion of the lipoids.

10-ml. portions of this emulsion were treated with 1 ml. of 11N-sulphuric acid and heated for varying periods in sealed tubes. After the heating phosphorus estimations were carried out. A determination of the total phosphorus content of the emulsion was also made.

The author expresses thanks to Professor A. R. Todd, F.R.S., and to Dr. E. Bergel for the gift of specimens of synthetic nucleotides.

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35. *The Oxidation of Aldoses by Hypoiodous Acid. Part III. Comparison of the Rates of Oxidation of α- and β-D-Glucose.*

By K. D. REEVE.

β-D-Glucose is shown to be oxidised by hypiodous acid, under certain conditions, at least 25 times as fast as is its α-isomer. The optimum pH for the observance of this difference in rates is 9·8 but the simultaneous mutarotation tends to equalise the two rates as oxidation proceeds. Outside the pH range 7·6—11·8, the α- and the β-form of D-glucose are oxidised at identical rates since under these conditions mutarotation is much faster than oxidation. The greater reactivity of β-D-glucose is in agreement with expectation.

OF the two pyranose forms of D-glucose, the β-form is generally the more reactive towards oxidising agents. The ratio v_β/v_α ($= r$) has been reported as 1·7 for oxidation by potassium permanganate (Kuhn and Wagner-Jauregg, *Ber.*, 1925, **58**, 1441) and 35 when bromine water is the oxidising agent (Isbell and Pigman, *Bur. Stand. J. Res.*, 1933, **10**, 337). For a wide variety of other aldoses values of r are greater than 1 for bromine-water oxidation (*idem, ibid.*, 1937, **18**, 141). Chlorous acid as an oxidising agent is anomalous in this respect, since r is less than 1 for hexoses (Jeanes and Isbell, *ibid.*, 1941, **27**, 125).

Since oxidations by iodine and bromine in aqueous solution are closely related it would be expected that r would be greater than 1 for both oxidation reactions. This has been assumed by Myrbäck (*Svensk Kem. Tidskr.*, 1940, **52**, 293) but since it has not hitherto been confirmed it was deemed desirable to test the validity of the assumption.

When either α- or β-D-glucose is oxidised in aqueous solution, a simultaneous mutarotation occurs, whereby an equilibrium solution containing 67% of the β- and 33% of the α-form is finally produced. If mutarotation is slow compared with oxidation a true measure of the ratio r can be obtained; otherwise the value of r will change during the reaction and its true initial value r^0 can be obtained only by extrapolation. The former conditions apply to bromine oxidation (Isbell and Pigman, *loc. cit.*, 1933), since the reaction is carried out at a pH (~6) where the mutarotation is slowest, while each oxidation reaction is conveniently fast. However, since the oxidising agent in aqueous iodine solutions is hypoiodous acid (Ingles and Israel, *J.*, 1948, 810), a higher pH must be employed in order to obtain a sufficient concentration of hypiodous acid for convenient oxidation rates. At these higher pH's, mutarotation rate is faster.

The variation of mutarotation rate with pH can be determined as follows. Mutarotation of D-glucose is catalysed by all Brønsted acids and bases. As the exact concentrations of all species in buffer solutions are not easy to assess, mutarotation constants have been calculated by taking into account the catalytic effects of H_2O, H_3O^+, and OH^- only. However, it has been shown that the contributions of bases such as pyrophosphate and carbonate ions are not negligible, by polarimetric measurements at 17·5° on a 5% solution of α-D-glucose at pH 8·8. The value of k_m was found to be 0·157, compared with the calculated value of 0·05 (see Table V). Thus minimum values are given in the tables.

The specific rate (k_m) of mutarotation under various conditions has been calculated from the equation

$$k_m = k_{H_2O} + k_{H_3O^+}[H_3O^+] + k_{OH^-}[OH^-]$$

data given by Smith and Smith (*J.*, 1937, 1413) being used. Table I gives some results of these calculations; others are in Table V.

TABLE I.

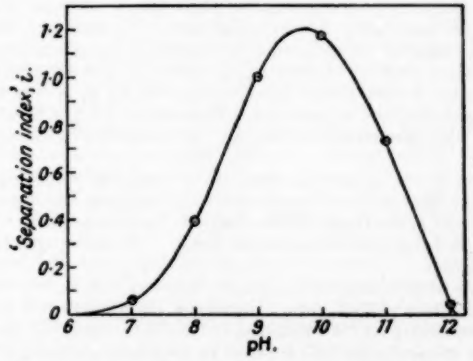
	k_m.				k_m.		
pH.	0°.	18°.	25°.	pH.	0°.	18°.	25°.
5	0·0017	0·0122	0·0240	10	0·0947	0·7167	1·160
6	0·0017	0·0123	0·0241	11	0·9317	7·057	11·38
7	0·0018	0·0129	0·0251	12	9·302	70·46	113·6
8	0·0026	0·0192	0·0354	13	93·00	704·5	1136·0
9	0·0110	0·0827	0·1376				

TABLE II.

pH	6	7	8	9	10	11	12
[HOI]	0·001*C*	0·01*C*	0·1*C*	*C*	9·8*C*	60·7*C*	35·7*C*
i	0·006	0·06	0·39	1·0	1·17	0·73	0·04

The optimum pH may be determined from comparative values of the " separation index " *i*. This is defined as proportional to the ratio of the initial velocities of oxidation of β-D-glucose and of mutarotation. For a constant concentration of sugar the latter is proportional to k_m and the former to the concentration of hypoiodous acid. The value of *i* is arbitrarily taken as 1 at pH 9 at 25°. Values of *i* at 25° at other pH can now be obtained from the equation $i = 0{\cdot}138[HOI]/k_mC$, where *C* is the concentration of hypoiodous acid at pH 9. The necessary comparative concentrations of hypoiodous acid in iodine–iodide solutions of constant concentration at various pH have been given by Ingles and Israel (*loc. cit.*). These and values of *i* are given in Table II.

FIG. 1.



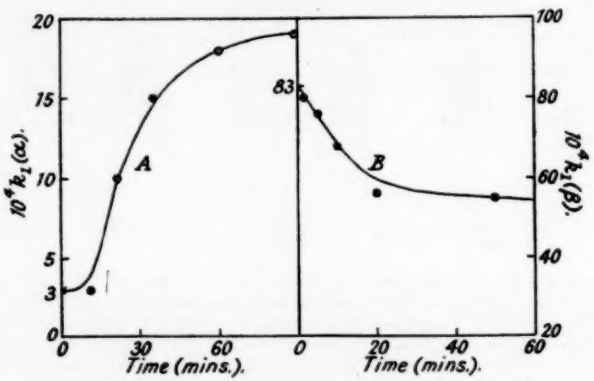
The plot of *i* against pH (Fig. 1) shows that *i* is a maximum at pH 9·8 and that outside the pH range 7·6—11·8 is less than 20% of this value. Under the latter conditions the two oxidation rates should be practically identical. Accordingly, oxidation experiments were carried out in solutions of pH as close as possible to 9·8.

The oxidation of D-glucose has been shown to be initially of the second order at pH 11·15 (Ingles and Israel, *J.*, 1949, 1249). At lower pH, iodate formation is negligible, so that the oxidation of each form should obey a second-order equation. Second-order velocity constants are calculated from the equation

$$k_2 = \frac{1}{T_\infty t} \log_e \frac{100 \times T_t}{U \times T_0}$$

where U = % of glucose unchanged and T is the sodium thiosulphate titre (see Experimental) at the time t. They decrease markedly during the oxidation of β-D-glucose and increase during the oxidation of α-D-glucose. The ratio r [$= k_2(\beta)/k_2(\alpha)$] is greater than unity at various times after reaction. The latter results show that β-D-glucose is the more readily oxidised form, and the former that mutarotation is interfering, as predicted, to cause the drifts in the values of k_2.

FIG. 2.



Extrapolations of velocity constants for Experiment 1, *Table* II.
- - - *A*, α-D-*Glucose*. *B*, β-D-*Glucose*.

The following extrapolation procedure was used to obtain r^0. First-order constants were calculated for the oxidation reaction in order to be compared with the first-order mutarotation constants, the equation used being $k_1 = (1/t)\log_e(100/U)$. Here also drifts similar to those described above were observed in each set of constants. The approximate determination of r^0 depends on obtaining a series of values for $k_1(\alpha)$ and $k_1(\beta)$ and extrapolating each set to zero time. The extrapolation is easy in the case of $k_1(\beta)$, but for $k_1(\alpha)$ it is not as definite and in many cases an extrapolation to 0 is indicated. However this is not justified and where values of $k_1^0(\alpha)$ are quoted they are maximum values. A typical set of extrapolations is shown in Fig. 2.

The accuracy of such extrapolations depends on obtaining values of the specific rates of oxidation at times when the amount of mutarotation is negligible, and is improved by measuring velocities during the very early stages of the reaction. Experiments at 1·5° have been useful, since both oxidation and mutarotation proceed slowly. However, this temperature is clearly about the lowest available.

A second possibility of obtaining more accurate values of r^0 is to increase the oxidation rates without increasing the mutarotation rate. Increasing the temperature was found to be in no way advantageous since any possible advantage obtained by increasing the oxidation rates in a greater ratio than the mutarotation rate is offset by decreased accuracy of measurement of the faster oxidation rates. Increasing the iodine concentration gives a slightly improved accuracy, but the necessary use of more iodide in concentrated iodine solutions results in the depression of iodine hydrolysis and the concentration of hypoiodous acid is not increased; there is thus little resultant advantage.

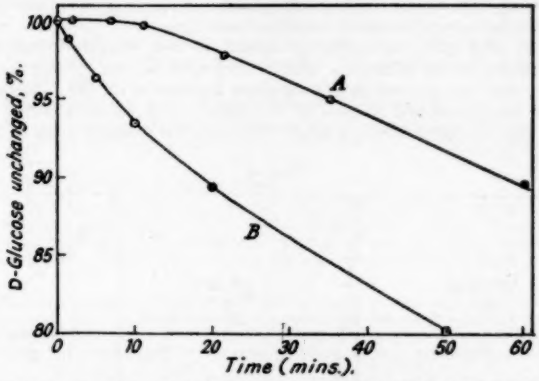
Results for seven experiments are summarised in Table III.

TABLE III.

Exp. no.	pH.	Temp.	$10^4k_1^0$ (min.$^{-1}$) α-.	β-.	r^0.	Exp. no.	pH.	Temp.	$10^4k_1^0$ (min.$^{-1}$) α-.	β-.	r^0.
1	9·2	1·5°	3	83	28	5	10·1	17·0°	800	10,000	13
2	9·2	1·5	5	137	28	6	8·4	35·0	1800	10,000	6
3	8·3	17·0	28	220	8	7	9·4	35·0	4000	16,000	4
4	8·8	17·0	90	1660	18						

Parts of the oxidation curves for experiment 1 are shown in Fig. 3. For reasons mentioned above and below (see " Materials " in the Experimental section) these values of r^0 cannot be regarded as accurate but are minimum values. It is in just those experiments (3, 6, 7) where measurements are least accurate that low values of r^0 are obtained.

FIG. 3.



Oxidation of α- (*A*) *and* β-D-*glucose* (*B*) *separately* (*Expt.* 1, *Table* III).

Thus as a first approximation it can be taken that D-glucose solution is oxidised by hypoiodous acid through the β-form and that α-D-glucose is itself not oxidised. From this it follows that the initial velocity constant k^0 (obtained by extrapolation) for various solutions should be proportional to the percentage of β-D-glucose in the solution. To test this, a mixture of equal weights of D-glucose samples containing 86% and 0% of β-D-glucose respectively was subjected to oxidation, and the initial velocity constant compared with that of the sample containing 86% of β-D-glucose. k^0 for the latter was 0·00360; for the mixture it should thus be 0·00180, in good agreement with the observed value of 0·00185.

It should also be possible to calculate approximate percentages of β-D-glucose in solution at various times during oxidation by extrapolating velocity constants to times other than $t = 0$. An experiment on α- or β-D-glucose included determination of the titre T and the percentage (U) of unchanged glucose, at about four time intervals. The percentage of β-D-glucose at time t_1 was found by using the equation

$$k_2 = \frac{1}{(t - t_1)T} \log_e \frac{U_1 T_t}{U_t T_1}, \quad \text{where } t = t_2, t_3, t_4.$$

The constants so obtained were extrapolated to give k_2 at time t_1.

From the equations

$$k_3 = \frac{1}{(t - t_2)T} \log_e \frac{U_2 T_t}{U_t T_2}, \quad \text{where } t = t_3, t_4$$

and

$$k_3 = \frac{1}{(t - t_3)T} \log_e \frac{U_3 T_t}{U_t T_3}, \quad \text{where } t = t_4$$

the values of k_3 at times t_2 and t_3 were obtained in a similar manner. These values of k_3 at 0, t_1, t_2, t_3 were then each taken as proportional to the percentage of β-D-glucose in each solution of experiment 1 (Table III) at the respective times, to give the values in Table IV.

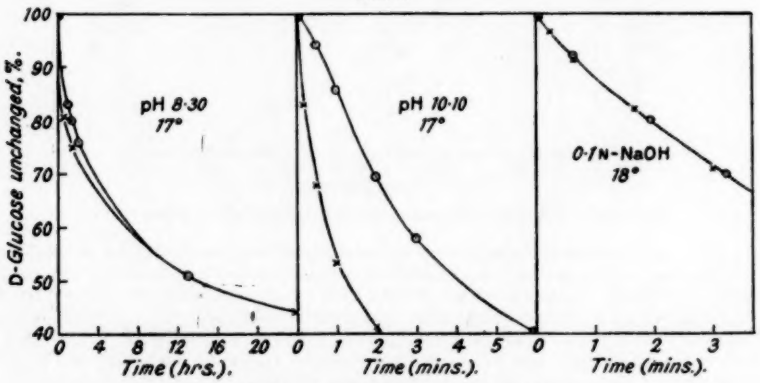
TABLE IV.

(*a*) β-D-Glucose, 86%.			(*b*) α-D-Glucose, 100%.		
t (mins.).	10^3k_1.	β-, %.	*t* (mins.).	10^3k_1.	β-, %.
0	3·6	86	0	0·10	2·5
5	3·4	81	11	0·80	20
10	2·2	55	21·5	0·96	24
20	2·2	55	35	1·13	28

These values show that the normal equilibrium solution containing 67% of β-D-glucose is not attained during reaction, but since β-D-glucose is oxidised preferentially a dynamic equilibrium is reached in which the percentage of this isomer is much less than that in the normal equilibrium solution. In case (*b*) β-D-glucose is oxidised almost as soon as it is formed through mutarotation, and hence the increase in the percentage of this isomer is slower than its decrease in case (*a*) where both mutarotation and oxidation reactions combine in impoverishing the solution in the more reactive form.

At a sufficiently high pH, mutarotation should be fast enough to maintain the normal equilibrium percentages in the solution. This is shown to be true by the identity of the rates of oxidation of α- and β-D-glucose in 0·1N-sodium hydroxide at 18°. Similarly, the normal equilibrium would be maintained in neutral or slightly acid solution owing to the very slow oxidation rates. Fig. 4 summarises the effect of pH on the relative rates of oxidation.

FIG. 4.



Oxidation of α- and β-D-glucose separately.

⊙ α-D-*Glucose.* × β-D-*Glucose.*

Further evidence may be obtained by considering the figures of Table V (expt. numbers refer to Table III).

TABLE V.

Expt. no.	k_m.	k_1^0 (β).	k_1^0 (α).	k_m/k_1^0 (α).	Expt. no.	k_m.	k_1^0 (β).	k_1^0 (α).	k_m/k_1^0 (α).
1	0·01	0·014	0·0005	20	5	0·90	1·0	0·08	11
2	0·01	0·008	0·0003	33	6	0·14	1·0	0·18	0·8
3	0·03	0·022	0·0028	11	7	0·60	1·6	0·40	1·5
4	0·05	0·165	0·009	6					

It may be noted that in all cases but one the oxidation rate of α-D-glucose is less than the mutarotation rate. This is in agreement with the hypothesis that α-D-glucose must await mutarotation to β-D-glucose before being oxidised, since $k_1^0(\alpha)$ must not exceed k_m. On the other hand, k_m is never negligible in comparison with $k_1^0(\beta)$. The case where $k_1^0(\alpha) > k_m$ is probably caused by the calculated value of k_m being much too low.

The necessary conditions for accurate assessment of $k_1^0(\beta)$ and $k_1^0(\alpha)$ would be $k_m < k_1^0(\alpha) < k_1^0(\beta)$. $k_1^0(\alpha)$ could not be shown to be zero unless mutarotation could be reduced to zero.

The great difference in the rates of oxidation of α- and β-D-glucose by bromine water has

been traced to a steric factor by Isbell and Pigman (*loc. cit.*, 1933). A similar mechanism may also apply to hypoiodous acid oxidations.

Experimental.

Buffers.—Buffers used included those described in Part I of this series, sodium pyrophosphate–hydrochloric acid buffers (Israel and Reeve, *Australian Chem. Inst. J. and Proc.*, 1949, **16**, 97) and a phosphate buffer (Sørensen, cf. Britton, "Hydrogen Ions," Chapman and Hall, 1932, p. 241). All solutions were checked for pH after addition of the iodine to the buffer at the temperature of reaction, by using a pH electrometer (N. L. Jones, Melbourne) standardised against 0·05M-sodium borate (pH 9·25 at 20°). The interference in the reaction of the usual buffers for the pH range 8·8—10·1 (Ingles and Israel, *J.*, 1948, 810) prevented measurements in this range.

Materials.—Materials used were of Analytical Reagent grade, except α- and β-D-glucose. α-D-Glucose used was a B.D.H. sample and when checked polarimetrically gave an initial value of 112·0° for $[\alpha]_D^{20}$ (Bates, "Polarimetry and Saccharimetry of Sugars," U.S. Dept. of Commerce, gives 112·2° for α-D-glucose), indicating that the sample was pure. β-D-Glucose was prepared by treating D-glucose for several minutes with boiling pyridine, cooling the mixture, and filtering off the precipitated β-D-glucose–pyridine complex. The pyridine was driven off in an air-oven at 105° and the sample placed in a vacuum-desiccator for several hours (Beilstein, Vol. XXXI, p. 87). When checked polarimetrically an initial specific rotation of 31·8° was obtained (Bates, *op. cit.*, gives 18·7°), indicating an 86% content of β-D-glucose.

The $[\alpha]_D^{20}$ of equilibrium solutions of both sugars was 52·6° (Bates gives 52·7°).

The impurity of the β-D-glucose used would indicate a slight correction (+16%) to r^0 but the accuracy of values in Table III is not high enough for such a correction to have much significance. Thus r^0 in Table III is uncorrected.

Kinetic Methods.—Two general methods were used.

(*a*) Where the oxidation was slow enough, solid glucose was added to a mixture of buffer and iodine solution kept within 0·1° of the temperature stated. For 1·5°, an ice–water bath was used. A required amount of this solution was withdrawn at various times and run into 3% sulphuric acid (50 ml.). The liberated iodine was titrated against 0·02N-sodium thiosulphate (microburette).

(*b*) The above technique was not satisfactory when the oxidation rate was fast, since the glucose takes a finite time to dissolve. In these cases a separate flask was used for each determination. The glucose was dissolved in a standard amount of distilled water and as soon as possible added to the reaction flask. A stock solution of glucose could not be used since a complete experiment occupied about half an hour.

In each case the residual iodine titre at the end of the reaction was determined by making the solution alkaline with 0·1N-sodium hydroxide, the reaction then proceeding to completion within a few minutes.

The following is a summary of the techniques used for each experiment of Table III:

Expt. no.	Buffer type.	Technique.	Buffer, ml.	I_2 soln., ml.	Sample withdrawn, ml.	I_2 soln., M.	Glucose, g.
1	Pyrophosphate	(*a*)	150	50	25	0·050	0·2
2	,,	(*a*)	150	50	25	0·100	0·2
3	Phosphate	(*a*)	50	55	10	0·037	0·2
4	Pyrophosphate	(*a*)	150	50	25	0·037	0·2
5	Carbonate	(*b*)	15	5	—	0·037	0·02
6	Pyrophosphate	(*b*)	15	5	—	0·037	0·02
7	Carbonate	(*b*)	15	5	—	0·037	0·02

The author thanks Dr. J. B. Polya and Mr. G. C. Israel for assistance given through helpful discussions and suggestions.

University of Tasmania, Hobart. [*Received, August 2nd*, 1950.]

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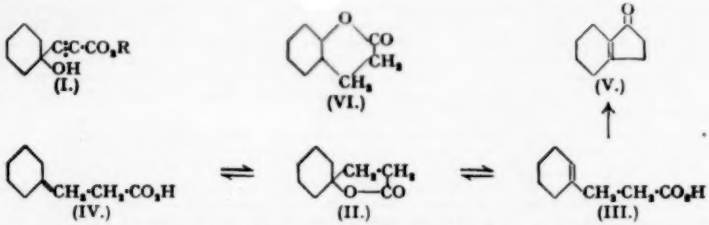
36. *Perhydroindanes. Part I. Some Products from 1-Hydroxycyclohexylpropiolic Acid.*

By David W. Mathieson.

The synthesis is described of 4 : 5 : 6 : 7-tetrahydroindan-1-one from *γ-cyclo*hexane*spiro*butyrolactone and some related products.

In connection with the synthesis of perhydroindanes the investigation was undertaken of certain methods for the introduction of a propionic acid residue in place of the carbonyl-oxygen atom of a pre-formed *cyclo*hexanone nucleus. The difficulties and side reactions besetting

attempts to utilise ethyl β-bromopropionate in a Reformatsky-type reaction prompted an approach *via* the readily available 1-hydroxy*cyclo*hexylpropiolic acids. After this work had been completed, Bachmann and R[illegible] (*J. Amer. Chem. Soc.*, 1950, **72**, 2530) reported work along similar lines.



In place of a one-stage condensation utilising methyl sodiopropiolate (Bachmann and Raunio, *loc. cit.*), the synthesis of the required propiolic acid (I; R = H) has been carried out in two stages. *cyclo*Hexanone was converted into ethynyl*cyclo*hexanol which was carboxylated as described by Jones and Whiting (*J.*, 1949, 1423), to yield the known 1-hydroxy*cyclo*hexylpropiolic acid (I; R = H). Hydrogenation of this in ethyl acetate with Adams's platinum oxide led to the rapid uptake of two moles of hydrogen and the subsequent isolation of crystalline γ-*cyclo*hexane*spiro*butyrolactone (II). From the mother-liquors *cyclo*hexylpropionic acid was isolated as *p*-bromophenacyl ester, presumably produced by dehydration of the β-1-hydroxy*cyclo*hexylpropionic acid during the somewhat exothermic saturation of the triple bond.

In view of Johnson, Petersen, and Sneider's work (*J. Amer. Chem. Soc.*, 1947, **69**, 74), the possibility was considered that the *spiro*lactone (II) in presence of acids would exist in equilibrium with β-*cyclo*hex-1-enylpropionic acid (III) and possibly with *cyclo*hexylidenepropionic acid

Substance.	Conditions.	Products, %. Acid (IV).	Lactone (II).
(II)	$KHSO_4$, 200°, 45 mins.	14	80
	$(CO_2H)_2$, 200°, 60 mins.	16	80
	Reagent A,* 4 hrs. (reflux)	2	94
	,, 8 hrs. ,,	2	93
(III)	Reagent A, 4 hrs. ,,	30	65
	,, 8 hrs. ,,	10	82
(IV)	Reagent A, 4 hrs. ,,	57 (mixture)	33

* AcOH : HCl : H_2O = 7 : 3·5 : 5 parts by vol. (Johnson, Petersen, and Sneider, *loc. cit*).

(IV). The lactone (II) was therefore treated with certain acid reagents as described in a preliminary note (Linnell and Mathieson, *Nature*, 1950, **165**, 1010), and at the same time equilibration of the other two possible tautomerides was investigated in like fashion. The results, shown in the table, agree with those of Johnson and Hunt (*J. Amer. Chem. Soc.*, 1950, **72**, 935), whose paper prompted the publication of our note. Linstead, Wang, Williams, and Errington (*J.*, 1937, 1136) record a 50% conversion of *cyclo*hexylidenepropionic acid (IV) into the *spiro*lactone in presence of 50% sulphuric acid after 4 hours at room temperature. The acid fraction from *cyclo*hexylidenepropionic acid is complex. Although isomerism of (IV) to β-*cyclo*hexylacrylic acid is known to occur under the influence of alkali, it is possible, as pointed out by Johnson and Hunt (*loc. cit.*), that this change also occurs under acid conditions. In addition, however, it is shown below that ring closure of (IV) with acid reagents affords 4 : 5 : 6 : 7-tetrahydroindan-1-one in 5% yield. Since ring closure must presumably take place *via* β-*cyclo*hex-1-enylpropionic acid (III), the presence of this acid—in addition to β-*cyclo*hexylacrylic acid—is likely in the acid fraction.

As the equilibrium (II) ⇌ (III) under acid conditions was so far in favour of the lactone (II), direct conversion of the latter into the indanone (V) seemed likely to be disappointing. Ring closure of such *spiro*lactones must proceed *via* the intermediate β-*cyclo*hexenylpropionic acids, and the work of Johnson *et al.* (*J. Amer. Chem. Soc.*, 1945, **67**, 1366; 1947, **69**, 74) has shown that where the acid-catalysed equilibrium mixture contains a significant proportion of the enoic acid, ring closure of a sample of the *spiro*lactone by Fieser and Hershberg's method (*J. Amer. Chem. Soc.*, 1937, **59**, 1028) proceeds in fair yield. As expected in the present case, ring closure of (II) to form (V) could be achieved in only 16% yield with

phosphoric oxide in benzene, or 7·5% with zinc chloride–acetic anhydride–acetic acid (yields being based on semicarbazone isolated from the reaction mixture). The structure of the ketone (V), previously described by Nenitzescu and Przmetsky (*Ber.*, 1941, **74**, 676), was confirmed by the fact that its 2 : 4-dinitrophenylhydrazone showed maximum absorption at 388 mμ., as required for an αβ-unsaturated ketone (Braude and Jones, *J.*, 1945, 498).

By Cason, Adams, Bennett, and Register's method (*J. Amer. Chem. Soc.*, 1944, **66**, 1764), the lactone (II) yielded ethyl β-*cyclo*hex-1-enylpropionate as described by Johnson and Hunt (*loc. cit.*). Hydrolysis of this, however, proved disappointing. With aqueous sodium hydroxide, the acid resulted in 16% yield (identified by comparison of its *p*-bromophenacyl ester with a sample synthesised by Arndt–Eistert homologation of *cyclo*hexenyl-1-acetic acid). The remainder of the hydrolysis product was a lactone of the same empirical formula and melting point, but it had a different crystalline form, and on admixture with the lactone (II) it immediately liquefied. It is tentatively assigned the constitution of a δ-lactone (VI), a substance described as an oil by Nenitzescu and Przmetsky (*loc. cit.*). Attempted hydrolysis of ethyl β-*cyclo*hex-1-enylpropionate with 4N-hydrochloric acid gave 8% of the required acid (III) and, mainly, the lactone (II).

Ring closure of the acid (III) with zinc chloride–acetic anhydride–acetic acid afforded the indanone (V) in 37% yield (based on once recrystallised semicarbazone).

Several modifications in the above reactions were equally fruitless. (i) The methyl ester of the acid (I) behaved similarly to the acid itself, yielding on reduction a mixture of the *spiro*-lactone (II) and methyl β-*cyclo*hexylpropionate. (ii) Treatment of the *spiro*lactone (II) with the theoretical amount of sodium hydroxide gave sodium β-1-hydroxy*cyclo*hexylpropionate, but treatment of this with phosphorus pentachloride and then stannic chloride (cf. Haberland and Heinrich, *Ber.*, 1939, **72**, 1215; 1943, **76**, 621) failed to afford any ketone.

Experimental.

γ-cyclo*Hexane*spiro*butyrolactone*.—1-Hydroxy*cyclo*hexylpropiolic acid (Jones and Whiting, *loc. cit.*) (50 g.) in ethyl acetate (250 ml.) was shaken with hydrogen under laboratory conditions in presence of Adams's platinum oxide (0·5 g.). Uptake of hydrogen, which was exothermic, was complete in 2 hours. Evaporation of the filtered solution yielded an oil, b. p. 125°/5 mm., n_D^{20} 1·4765 (supercooled specimen) (46 g., 98%). When this was kept overnight at 0°, large colourless prisms separated; recrystallised from light petroleum (b. p. 40—60°), they had m. p. 28—29° (Linstead, Wang, Williams, and Errington, *loc. cit.*, give m. p. 20—25° for a sample synthesised by an alternative route) (Found : C, 70·5; H, 9·2%; sap. equiv., 154. Calc. for $C_8H_{14}O_2$: C, 70·0; H, 9·1%; sap. equiv., 154). By dissolving the *spiro*lactone in the theoretical amount of aqueous barium hydroxide and concentrating the solution, *barium β-hydroxy*cyclo*hexylpropionate* was obtained (Found : Ba, 28·6. $C_{16}H_{30}O_6Ba$ requires Ba, 28·6%).

The mother-liquors after removal of the crystalline lactone showed an acid fraction 31% by weight on direct titration in 40% aqueous methanol against N/10-sodium hydroxide. The oil failed to decolorise aqueous potassium permanganate or bromine in carbon tetrachloride, and was transparent to light of 215 mμ., unlike 1-hydroxy*cyclo*hexylpropiolic acid (Haynes and Jones, *J.*, 1946, 503). The acid fraction, separated by extraction with sodium hydrogen carbonate, was a colourless oil, b. p. 115—120°/2 mm. (bath-temp.). Chromatography on alumina of the derived *p*-bromophenacyl ester yielded the p-*bromophenacyl* ester of *β-cyclo*hexylpropionic acid, m. p. 93—94° (from light petroleum). It was identified by mixed m. p. with an authentic specimen (see below) (Found : Br, 22·4. $C_{17}H_{21}O_3Br$ requires Br, 22·6%).

Hydrogenation of Methyl 1-*Hydroxy*cyclo*hexylpropiolate*.—The methyl ester (13·4 g.) was hydrogenated in presence of Adams's platinum oxide (0·1 g.) as described for the free acid. The resulting material yielded two fractions : (*a*) B. p. 37—38°/0·05 mm., 3·46 g. (27%), n_D^{20} 1·4475 (Found : C, 70·9; H, 10·8%; sap. equiv., 169. Calc. for $C_{10}H_{18}O_2$: C, 70·6; H, 10·6%; sap. equiv., 170); this was methyl *β-cyclo*hexylpropionate, and on hydrolysis with 20% sodium hydroxide it afforded an acid, b. p. 115—118°/3 mm., of which the *p*-bromophenacyl ester, formed in the usual way, had m. p. and mixed m. p. with *p*-bromophenacyl *β-cyclo*hexylpropionate 93—94°. (*b*) B. p. 70—72°/0·05 mm., 5·87 g. (49%), n_D^{20} 1·4758, m. p. 24—25° not depressed on admixture with γ-*cyclo*hexane*spiro*butyrolactone.

1-*cyclo*Hexenylacetic acid, prepared (80% yield) by iodine dehydration of ethyl 1-hydroxy*cyclo*hexylacetate followed by hydrolysis, had b. p. 94—95°/0·1 mm., m. p. 35—36°.

β-cyclo*Hex*-1-*enylpropionic Acid*.—*cyclo*Hexenylacetic acid (26 g.) in dry benzene (50 ml.) was added, with stirring, to pure thionyl chloride (35 ml.) during 2 hours, and the whole heated under reflux for 30 minutes; excess of solvent and reagent was removed *in vacuo*, and the residual acid chloride distilled (b. p. 60—65°/3 mm.; 25 g.). It was dissolved in dry ether and treated overnight at 0° with an ethereal solution of diazomethane (800 ml.) (from *N*-nitrosomethylurea, 37 g.). Evaporation of the solvent yielded an oily yellow diazo-ketone (27 g.) which in dry dioxan (60 ml.) was slowly added to a stirred solution of freshly precipitated silver oxide (25 g.) and sodium thiosulphate (30 g.) in water (300 ml.). After the addition was complete, stirring was continued at 40° for 1½ hours, the mixture was filtered, and the mother-liquors were acidified with dilute nitric acid to yield an oil which was extracted with ether.

Purification of this acid fraction *via* the sodium salt yielded *β-cyclo*hex-1-enylpropionic acid as a colourless oil, b. p. 88—91°/0·1 mm., n_D^{20} 1·4884; 11·02 g. (38%) (Found: C, 69·5; H, 9·4%; equiv., 154. Calc. for $C_9H_{14}O_2$: C, 70·0; H, 9·1%; equiv., 154). The p-*bromophenacyl* ester crystallised from ethanol in colourless plates, m. p. 108—109° (Found: Br, 22·2. $C_{17}H_{19}O_3Br$ requires Br, 22·7%).

β-cyclo*Hexylpropionic Acid.*—*β-cyclo*Hex-1-enylpropionic acid (1 g.) in ethanol (10 ml.) was hydrogenated in presence of Adams's platinum oxide (0·1 g.), uptake being complete in 20 minutes. The product, a colourless oil, b. p. 90—91°/0·2 mm., n_D^{17} 1·4665, gave a *p*-bromophenacyl ester crystallising from light petroleum (b. p. 60—80°) in colourless plates, m. p. 92—93° (Found: Br, 22·3%).

*β-cyclo*Hexylidenepropionic acid was synthesised by the method of Linstead, Wang, Williams, and Errington (*loc. cit.*).

Equilibration Studies.—General procedure. A sample of the material under investigation (1 g.) was heated with the reagent used [twice its weight of anhydrous oxalic acid or potassium hydrogen sulphate, or reagent A (15 ml.; see p. 178)] for the times and at the temperatures stated in the table (p. 178). After addition of water (10 ml.), or evaporation of the acetic acid in the last case, an ethereal extract was separated into neutral and acidic fractions by sodium hydrogen carbonate extraction. The constituents were then identified as follows: *γ-cyclo*hexane*spiro*butyrolactone by b. p., m. p., refractive index, and saponification equivalent; *β-cyclo*hex-1-enylpropionic acid by equivalent (titration) and formation of its *p*-bromophenacyl ester. Equilibration of both these compounds yielded substantially pure end-products. The *p*-bromophenacyl ester of the acid fraction from *β-cyclo*hexylidenepropionic acid (IV) had m. p. 96—109° not raised by further recrystallisation from ethanol or light petroleum.

Ethyl *β-cyclo*hex-1-enylpropionate, prepared (yield 76%) essentially as described by Johnson and Hunt (*loc. cit.*), had b. p. 83—85°/3 mm., n_D^{15} 1·4656 (Found: C, 72·4; H, 10·0%; sap. equiv., 181. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·9%; sap. equiv., 182).

Alkaline hydrolysis. Ethyl *β-cyclo*hex-1-enylpropionate (2 g.), 10% sodium hydroxide solution (10 ml.), and ethanol (3 ml.) were refluxed for 40 minutes, by which time the oily layer had passed into solution. After acidification, both the acidic and the lactonic fraction were removed by ether-extraction, then separated with sodium hydrogen carbonate in the usual way. There thus resulted: (*a*) An acid fraction, 282 mg. (16%), equiv. by titration, 154; *p*-bromophenacyl ester, m. p. 107—108° undepressed on admixture with the corresponding ester of *β-cyclo*hex-1-enylpropionic acid. (*b*) A neutral fraction with a typical lactonic odour (1·18 g., 75%), slowly soluble in sodium hydroxide on warming. When it was cooled in carbon dioxide–acetone, colourless needles were obtained, m. p. 29—30° (from light petroleum, b. p. 40—60°) (Found: C, 69·6; H, 9·2%; sap. equiv., 151. $C_9H_{14}O_2$ requires C, 70·0; H, 9·1%; sap. equiv., 154); on admixture with a sample of *γ-cyclo*hexane*spiro*butyrolactone, the whole immediately liquefied.

Acid hydrolysis. Ethyl *β-cyclo*hex-1-enylpropionate (1·35 g.) was refluxed for 3 hours with 4N-hydrochloric acid (15 ml.). After separation there resulted: (*a*) Acid fraction, 80 mg. (8·7%); *p*-bromophenacyl ester, m. p. 106—108°, undepressed on admixture with *p*-bromophenacyl *β-cyclo*hex-1-enylpropionate. (*b*) Lactonic fraction, 0·96 g. (83%), b. p. 130—135°/10 mm. (bath-temp.), n_D^{20} 1·4745; after this had solidified in a carbon dioxide–acetone bath, several recrystallisations from light petroleum (b. p. 60—80°) gave *γ-cyclo*hexane*spiro*butyrolactone, m. p. and mixed m. p. with an authentic specimen 28—29°.

Ring-closure Experiments.—(i) *β*-cyclo*Hex-1-enylpropionic acid.* This acid (5 g.) in acetic anhydride (85 ml.) was refluxed for 4 hours in a nitrogen atmosphere with a 2% solution of anhydrous zinc chloride in acetic acid (20 ml.). The solution was then concentrated to half bulk, and any residual anhydride decomposed by shaking the mixture with ice and excess of 20% sodium hydroxide solution. The alkaline liquors were steam-distilled till the distillate no longer gave a positive reaction with 2 : 4-dinitrophenylhydrazine. The distillate, saturated with sodium chloride, was thoroughly extracted with ether, and the dried extract evaporated. The residue distilled at 85—90°/0·5 mm. (bath-temp.) (2·28 g., 51·5%) and proved to be 4 : 5 : 6 : 7-tetrahydroindan-1-one. The semicarbazone from the above (2·3 g.; 37% yield based on this derivative) crystallised in pale yellow needles, m. p. 245—246° (placed in bath at 235°) (Found: N, 21·4. Calc. for $C_{10}H_{15}ON_3$: N, 21·7%), from aqueous acetic acid. The 2 : 4-dinitrophenylhydrazone crystallised in dark red needles, m. p. 238°, from ethanol; $\lambda_{max.}$ 388 mμ., $\varepsilon_{max.}$ 27,000; Johnson, Hunt, and Stork (*J. Amer. Chem. Soc.*, 1948, **70**, 3022) give m. p. 242·5—243° and 238—239·5°, respectively, for the semicarbazone and dinitrophenylhydrazone.

(ii) *γ*-cyclo*Hexane*spiro*butyrolactone.* (*a*) The *spiro*lactone (17·15 g.) in acetic anhydride (300 ml.) with zinc chloride solution (as above; 100 ml.) was refluxed for 4 hours in a nitrogen atmosphere; after working up as described above there resulted 4 : 5 : 6 : 7-tetrahydroindan-1-one as a light yellow oil, b. p. 60—65°/0·05 mm. (bath-temp.), 2·02 g. (13%); 2 g. of crystalline semicarbazone were obtained from this material as small, pale yellow needles (from dilute acetic acid), m. p. 245—246°. (*b*) The *spiro*lactone (2 g.) in dry benzene (50 ml.) was refluxed for 2½ hours with phosphoric oxide (4 g.) and an equal bulk of acid-washed kieselguhr. The dark viscous residue was decomposed by addition of water, the benzene layer was removed, and the aqueous layer extracted with benzene. Evaporation of the combined extracts gave a residue which was warmed for 2 hours on the steam-bath with 10% sodium hydroxide to cleave any lactone. Non-alkali-soluble material was extracted with benzene to yield the required ketone, 463 mg. (24·6%), b. p. 60—67°/0·05 mm., which gave a semicarbazone (400 mg.), m. p. 245—246°, from aqueous acetic acid (16% yield based on semicarbazone).

(iii) *β*-cyclo*Hexylidenepropionic acid.* The acid (2 g.), acetic anhydride (35 ml.), and stock solution of zinc chloride (12 ml.) were refluxed for 4 hours. There resulted after working up as above 314 mg. of a light yellow oil, from which 115 mg. of semicarbazone were obtained, m. p. 243—245° (from aqueous acetic acid) (4·6% yield based on semicarbazone).

All m. p.s are uncorrected. Absorption spectra were determined by use of a " Uvispek " photoelectric spectrophotometer and a cell-path of 1 cm., with ethanol as solvent. Microanalyses were carried out by Mr. G. S. Crouch.

The author thanks the University of London for the award of an I.C.I. Fellowship during the tenure of which the above work was carried out, and Professor W. H. Linnell for much help.

School of Pharmacy, University of London. [*Received, August 3rd*, 1950.]

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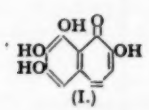
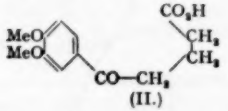
37. 4-*Hydroxy*-2′ : 3′-*dimethoxybenz*cyclo*heptatrien*-3-*one and Related Topics.*

By J. A. Barltrop, A. J. Johnson, and G. D. Meakins.

Dehydrogenation of 2′ : 3′-dimethoxybenz*cyclo*heptene-3 : 4-dione (V) has been shown to give rise to the dimethoxybenztropolone (VI). Certain intermediates of potential value for the synthesis of benztropolones are described.

The recent publication by Caunt, Crow, Haworth, and Vodoz (*J.*, 1950, 1631), which provides synthetical proof of the correctness of the benztropolone structure (I) for purpurogallin, originally suggested by Barltrop and Nicholson (*J.*, 1948, 116), also describes the synthesis of the dimethoxybenztropolone (VI). We synthesised this compound some time ago, but withheld publication while attempts were made to extend the method to the synthesis of purpurogallin itself. In view of this communication by Haworth *et al.* it would seem desirable to submit an account of our own work in this field.


(I.)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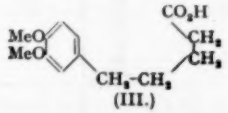
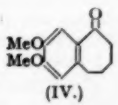

(III.)

γ-(3 : 4-Dimethoxybenzoyl)butyric acid (II) was prepared in 83% yield by condensing glutaric anhydride with veratrole in the presence of aluminium chloride, excess of veratrole being used as solvent. This procedure constitutes an improvement on that described by Caunt, Crow, Haworth, and Vodoz (*loc. cit.*) who obtained the product in 55% yield. The reduction of (II) using Martin's modification of the Clemmensen method (*J. Amer. Chem. Soc.*, 1936, **58**, 1438) gave an almost quantitative yield of δ-(3 : 4-dimethoxyphenyl)valeric acid (III). Catalytic reduction of the keto-acid was also studied. By using freshly prepared Raney nickel catalyst under carefully controlled conditions, the reduction was effected in 82% yield. Presumably, δ-(3 : 4-dimethoxyphenyl)-δ-valerolactone (VII) is involved as an intermediate; indeed, this compound can be isolated by performing the hydrogenation over palladised charcoal at atmospheric pressure and temperature.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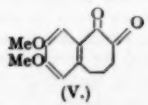
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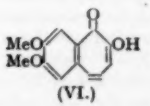
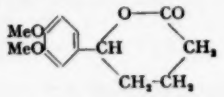
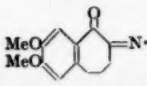

(VI.)

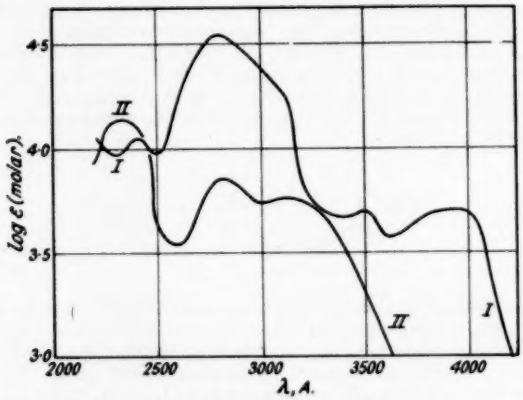
The cyclisation of δ-phenylvaleroyl chloride to benz*cyclo*heptenone by the usual methods has been reported to proceed in yields varying between 27% and 50% (Kipping and Hunter, *J.*, 1901, **79**, 602; Borsche and Roth, *Ber.*, 1921, **54**, 174; Kadesch, *J. Amer. Chem. Soc.*, 1944, **66**, 1207), but by using a high-dilution technique, Plattner (*Helv. Chim. Acta*, 1944, **27**, 801) was able to raise the yield to 87%. This last method, applied to δ-(3 : 4-dimethoxyphenyl)valeroyl chloride, effected an extremely satisfactory conversion into 2′ : 3′-dimethoxybenz*cyclo*hepten-3-one (IV), but the procedure, involving the prolonged stirring of large quantities of boiling carbon disulphide, was clearly ill-suited to the production of (IV) in quantity. A more convenient method was found to be the cyclodehydration of the parent acid by means of phosphoric oxide in benzene solution. Distillation of (III) with zinc chloride in a high vacuum gave only small yields of a somewhat impure material.

Our own preliminary experiments suggested that the 2′ : 3′-dimethoxybenz*cyclo*hepten-3-one could be neither oxidised smoothly with selenium dioxide to the diketone (V), nor readily nitrosated with *iso*amyl nitrite and sodium ethoxide. However, it was found that nitrosation under carefully controlled conditions in the presence of hydrogen chloride afforded the 4-oximino-2′ : 3′-dimethoxybenz*cyclo*hepten-3-one (VIII) in virtually quantitative yield.

(VII.) 


(VIII.)

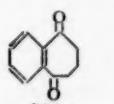
Although the oximino-ketone could be transformed into the diketone (V) by prolonged warming with nitrous acid, subsequent experiments revealed that hydrolysis by dilute hydrochloric acid in the presence of formaldehyde was much better. Haworth *et al.* (*loc. cit.*) encountered difficulty in effecting this hydrolysis and obtained the dione as an oil. We find the compound to be a highly crystalline solid, m. p. 104°.

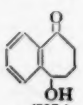


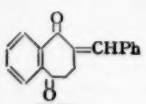
I. 4-*Hydroxy*-2′ : 3′-*dimethoxybenz*cyclo*heptatrien*-3-*one*.
II. 2′ : 3′-*Dimethoxybenz*cyclo*heptene*-3 : 4-*dione*.

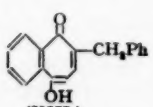
Dehydrogenation of the dione over palladised charcoal in boiling trichlorobenzene (cf. Cook and Somerville, *Nature*, 1949, **163**, 410) gave the dimethoxybenztropolone (VI) in 8% yield. The substance appears to be identical with that described by Haworth *et al.*; it resembles all other known tropolones in forming no ketonic derivatives.

Some preliminary experiments have been made to devise syntheses of tropolones avoiding the unsatisfactory dehydrogenation stage, which is a feature of all methods hitherto described. Benz*cyclo*heptene-3 : 7-dione (X), prepared by a modification of Dieckmann's method (*Ber.*, 1899, **32**, 2227), on hydrogenation, afforded a small quantity of 7-hydroxybenz*cyclo*hepten-3-one (XI), isolated as its semicarbazone. The dione (X) readily afforded a monobenzylidene derivative (XII), which from its large melting point range is presumably a mixture of geometrical isomers. Attempts to isomerise it to (XIII) have been unsuccessful.


(X.)

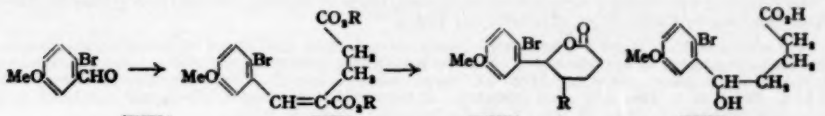

(XI.)


(XII.)


(XIII.)

A related approach involves the preparation of compounds of the general type (XI) from δ-(*o*-bromophenyl)valerolactones (XVI; R = H) by an intramolecular Grignard reaction. No

lactones of the type contemplated are known and their preparation by the following scheme was attempted :



(XIV.) (XV.) (XVI.) (XVII.)

2-Bromo-5-methoxybenzaldehyde (XIV), prepared in improved yield by a modification of Pschorr's method (*Annalen*, 1912, **391**, 23), would not condense with ethyl glutarate in the presence of either sodium, or sodium ethoxide. Potassium *tert.*-butoxide appeared to promote satisfactory reaction between (XIV) and ethyl glutarate but subsequent hydrolysis, decarboxylation, and lactonisation under the conditions used by Johnson (*J. Amer. Chem. Soc.*, 1945, **67**, 1357) in analogous condensations with ethyl succinate gave only a small amount of neutral material which was hydrolysed to δ-(2-bromo-5-methoxyphenyl)-δ-hydroxyvaleric acid (XVII). The low yield may be due to differences between the ease of formation of γ- and δ-lactones.

Fittig (*Annalen*, 1882, **216**, 99; 1889, **255**, 293) showed that substituted benzaldehydes, sodium succinate, and acetic anhydride condense to give phenylparaconic acids and phenyl*iso*crotonic acids, and that the paraconic acids may be transformed into the *iso*crotonic acids by pyrolysis. Condensation between (XIV) and sodium glutarate under similar conditions gave α-(2-bromo-5-methoxybenzylidene)glutaric acid (XV; R = H), a type of product finding no analogy in Fittig's work. The benzylidene-glutaric acid was expected to decarboxylate readily, but it was unaffected by pyrolysis, and copper-containing catalysts caused debromination. Mineral acids isomerised the acid (XV; R = H) to the lactone (XVI; R = CO_2H). Efforts to effect a decarboxylation and rearrangement of the lactone, analogous to the paraconic acid–*iso*crotonic acid transformation, have been unsuccessful.

Experimental.

γ-(3 : 4-*Dimethoxybenzoyl*)*butyric Acid.*—To a stirred, ice-cold solution of glutaric anhydride (10 g.) in veratrole (100 c.c.), finely pulverised aluminium chloride (26 g.) was added all at once and the stirring continued for one hour at 0°. After 15 hours at room temperature, the mixture was added to concentrated hydrochloric acid (100 c.c.) and ice and then extracted with chloroform. The organic layer was extracted with sodium carbonate solution and this on acidification precipitated γ-(3 : 4-dimethoxybenzoyl)butyric acid (18·5 g., 83%), m. p. 141—144°. After two recrystallisations from ethanol, the acid was obtained as colourless rhombs, m. p. 145—146° (Caunt, Crow, Haworth, and Vodoz, *loc. cit.*, give m. p. 140—145°) (Found : C, 61·6; H, 6·4. Calc. for $C_{13}H_{16}O_5$: C, 61·9; H, 6·4%).

δ-(3 : 4-*Dimethoxyphenyl*)*valeric Acid.*—(*a*) Concentrated hydrochloric acid (125 c.c.) was added to a boiling mixture of γ-(3 : 4-dimethoxybenzoyl)butyric acid (30 g.), amalgamated zinc (70 g.), water (60 c.c.), and toluene (100 c.c.) after 0, 6, and 18 hours. After being boiled for 36 hours, the reaction mixture was worked up in the usual manner. δ-(3 : 4-Dimethoxyphenyl)valeric acid (27·8 g., 97%) was obtained as a colourless solid, m. p. 72—74°.

(*b*) A solution of the keto-acid (5 g.) in ethanol (100 c.c.) was hydrogenated over freshly prepared Raney nickel catalyst at 80° and 50 atmospheres. After removal of the catalyst from the solution, and evaporation, trituration of the residue with light petroleum (b. p. 40—60°) gave the valeric acid (4 g., 82%), m. p. 71—74°.

δ-(3 : 4-*Dimethoxyphenyl*)-δ-*valerolactone.*—A solution of γ-(3 : 4-dimethoxybenzoyl)butyric acid (0·5 g.) in aqueous sodium hydroxide was hydrogenated for 16 hours over palladised-charcoal catalyst at room temperature and pressure. After removal of the catalyst, acidification, and isolation with ethyl acetate, δ-(3 : 4-*dimethoxyphenyl*)-δ-*valerolactone* was obtained as a clear glass, which, on being triturated with ether–light petroleum, gave colourless crystals, m. p. 156—159°. Two recrystallisations from ether–light petroleum furnished colourless prisms, m. p. 158—159° (Found : C, 65·7; H, 6·9. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

2′ : 3′-*Dimethoxybenz*cyclo*hepten*-3-*one.*—(*a*) Phosphorus pentachloride (2·4 g.) was added to a solution of δ-(3 : 4-dimethoxyphenyl)valeric acid (1·9 g.) in carbon disulphide (50 c.c.), and the mixture was refluxed for 30 minutes and then diluted with carbon disulphide (300 c.c.). The mixture was added dropwise during 30 hours to a vigorously stirred, gently boiling solution of stannic chloride (2·5 c.c.) in carbon disulphide (300 c.c.). After a further 5 hours, the solvent was distilled off, the complex decomposed with hydrochloric acid, and the product extracted with ether. The organic layer was washed with sodium carbonate solution, dried, and distilled. 2′ : 3′-Dimethoxybenz*cyclo*hepten-3-one (1·4 g., 80%) was collected as an almost colourless oil, b. p. 160—165° (bath temp.)/0·07 mm. It crystallised from ether–light petroleum in colourless needles, m. p. 63—64° (Found : C, 71·2; H, 7·4. Calc. for $C_{13}H_{16}O_3$: C, 70·9; H, 7·3%); dinitrophenylhydrazone, deep red-plates (glacial acetic acid), m. p. 226—227° (Found : C, 56·8; H, 4·9; N, 14·2. Calc. for $C_{19}H_{20}O_6N_4$: C, 57·0; H, 5·0; N, 14·0%). Haworth *et al.* (*loc. cit.*) obtained orange prisms, m. p. 234—236°. The semicarbazone formed prisms (from ethanol)

m. p. 205—206° (Found : C, 60·2; H, 6·8. Calc. for $C_{14}H_{19}O_3N_3$: C, 60·6; H, 6·9%) (Haworth *et al.* obtained needles, m. p. 190—192°).

(*b*) The acid was cyclised by means of phosphoric oxide in benzene solution with results similar to those described by Caunt, Crow, Haworth, and Vodoz.

4-*Benzylidene*-2′ : 3′-*dimethoxybenz*cyclo*hepten*-3-*one*.—A small quantity of sodium ethoxide dissolved in ethanol was added to a solution of 2′ : 3′-dimethoxybenz*cyclo*hepten-3-one (0·38 g.) and benzaldehyde (0·19 g.) in absolute ethanol. After 24 hours, 4-*benzylidene*-2′ : 3′-*dimethoxybenz*cyclo*hepten*-3-*one* (0·46 g., 90%), m. p. 154—156°, was collected. It separated from ethanol in pale-yellow needles, m. p. 157—158° (Found : C, 78·0; H, 6·4. $C_{20}H_{20}O_3$ requires C, 77·9; H, 6·5%).

2′ : 3′-*Dimethoxy*-4-*oximinobenz*cyclo*hepten*-3-*one*.—*iso*Amyl nitrite (5 g.) in dry ether (50 c.c.) was added dropwise during 2 hours to an ice-cold, stirred solution of 2′ : 3′-dimethoxybenz*cyclo*hepten-3-one (5 g.) in dry ether. Dry hydrogen chloride was passed into the mixture simultaneously. Stirring and the flow of hydrogen chloride were continued for a further ½ hour. Next morning the oximino-ketone hydrochloride (6·1 g., 95%) was collected; it formed a bright red solid. A solution of this in boiling water was neutralised and cooled. The oximino-ketone formed pale-yellow needles, m. p. 173° (Found : C, C, 62·6; H, 6·0. Calc. for $C_{13}H_{15}O_4N$: C, 62·6; H, 6·0%). Rapid cooling of the hot aqueous solution produced colourless crystals, m. p. 163—165°. The 2 : 4-*dinitrophenylhydrazone* crystallised from benzene in brick-red needles, m. p. 168—172° (decomp.) (Found : C, 53·6; H, 4·7. $C_{19}H_{19}O_7N_5$ requires C, 53·2; H, 4·4%).

2′ : 3′-*Dimethoxybenz*cyclo*heptene*-3 : 4-*dione*.—(*a*) A mixture of the oximino-ketone (2 g.), formaldehyde (10 c.c.; 40% aqueous solution), and 2N-hydrochloric acid (2 c.c.) was heated on the steam-bath for ten minutes. The deep-yellow solution, after being diluted with water (30 c.c.) and cooled, deposited 2′ : 3′-dimethoxybenz*cyclo*heptene-3 : 4-dione (1·65 g., 85%), which, recrystallised from boiling water, formed yellow leaflets, m. p. 104—105° (Found : C, 66·9; H, 6·0. Calc. for $C_{13}H_{14}O_4$: C, 66·7; H, 6·0%). It gave mono-2 : 4-dinitrophenylhydrazone, orange plates (from benzene), m. p. 247° (decomp.) (Found : C, 54·7; H, 4·0; N, 13·4. Calc. for $C_{19}H_{18}O_7N_4$: C, 55·1; H, 4·3; N, 13·5%) (Haworth *et al.*, *loc. cit.*, obtained yellow needles, m. p. 253°), and a *semicarbazone*, plates (from ethanol), m. p. 225—226° (Found : N, 14·1. $C_{14}H_{17}O_4N_3$ requires N, 14·4%). The diketone gave a deep-brown colour with ferric chloride and red solutions with alkali.

(*b*) The oximino-ketone (0·45 g.) was heated in a pressure bottle for 36 hours at 35—40° with sodium nitrite (1·2 g.), aqueous ethanol (100 c.c.; 50%), and concentrated sulphuric acid (1·2 c.c.). The solution was neutralised with sodium carbonate solution, concentrated under reduced pressure at 60°, filtered from the brown oil which separated first, and allowed to cool. The dione separated as yellow crystals (0·15 g., 37%), m. p. 95—97° raised to 104—105° by recrystallisation from water.

4-*Hydroxy*-2′ : 3′-*benz*cyclo*heptatrien*-3-*one*.—The dione (0·9 g.), 35% palladised charcoal (1·2 g.), and *s*-trichlorobenzene (15 c.c.) were refluxed in a stream of nitrogen for four hours. After being diluted with benzene, filtered from catalyst, and washed with sodium carbonate solution, the mixture was extracted with 2N-sodium hydroxide solution. Acidification precipitated the product which was isolated with chloroform and crystallised from water. The tropolone (0·06 g., 8%) was obtained as yellow needles, m. p. 145—146° (Found : C, 67·0; H, 5·1. Calc. for $C_{13}H_{12}O_4$: C, 67·2; H, 5·2%). It formed no ketonic derivatives, and dissolved in concentrated hydrochloric acid to a bright yellow solution from which it was precipitated unchanged by dilution.

*Benz*cyclo*heptene*-3 : 7-*dione*.—Ethyl phthalate (84 g.), ethyl glutarate (70·4 g.), and sodium wire (17·5 g.) were heated together in an oil-bath at 120—130° for four hours. The product was boiled for 36 hours with concentrated sulphuric acid (144 c.c.) and water (600 c.c.), and extracted with ethyl acetate. The organic layer was washed with sodium hydroxide solution, and distilled. Benz*cyclo*heptene-3 : 7-dione (19 g.) was collected at 173—176°/10 mm. The product slowly set to prisms, m. p. 45—46°.

7-*Hydroxybenz*cyclo*hepten*-3-*one*.—The 3 : 7-dione (0·5 g.) dissolved in ethanol was hydrogenated over palladised charcoal and a small proportion of Adams's catalyst at room temperature and pressure until one molar proportion of hydrogen had been absorbed. The solution after filtration and concentration gave a small yield of 7-hydroxybenz*cyclo*hepten-3-one, isolated as the *semicarbazone*, which separated from aqueous ethanol in prisms, m. p. 186—188° (Found : C, 61·3; H, 6·5. $C_{13}H_{15}O_3N_3$ requires C, 61·8; H, 6·4%).

4-*Benzylidenebenz*cyclo*heptene*-3 : 7-*dione*.—Benz*cyclo*heptene-3 : 7-dione (1·2 g.) and benzaldehyde (0·76 g.) were stirred at 0° for three hours with a solution of sodium hydroxide (0·36 g.) in water (10 c.c.) and ethanol (15 c.c.). After 12 hours, the solid was collected, washed with water, and dried. Two recrystallisations from ether–light petroleum gave 4-*benzylidenebenz*cyclo*heptene*-3 : 7-*dione* as a pale-yellow solid, m. p. 190—216° (Found : C, 82·1; H, 5·6. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·3%). The benzylidene compound, when heated with alkali under varying conditions, gave traces of alkali-soluble material which could not be purified.

2-*Bromo*-5-*methoxybenzaldehyde*.—A mixture of 2-bromo-5-hydroxybenzaldehyde (50 g.), potassium carbonate (40 g.), methyl iodide (40 c.c.), and dry acetone (300 c.c.) was heated under reflux for eight hours, more methyl iodide (20 c.c.) being added after four hours. The mixture was filtered and the insoluble solids twice washed with boiling acetone. The combined filtrates were evaporated to dryness and the product (43 g., 80%) isolated with ether. It separated from methanol in crystals, m. p. 72—73°.

Condensation of Ethyl Glutarate with 2-*Bromo*-5-*methoxybenzaldehyde*.—A solution of potassium (2 g.) in *tert.*-butanol (50 c.c.) was refluxed in a nitrogen atmosphere with the aldehyde (10 g.) and ethyl glutarate (16·4 c.c.). After 40 minutes, concentrated hydrochloric acid (9·5 c.c.) in water (46 c.c.) and salt were added, and the butanol layer was separated off and concentrated under reduced pressure. The product, a dark liquid, was dissolved in ether and extracted with 5% potassium carbonate solution. The

aqueous layer was acidified and then extracted with ether, the extract being washed with water and brine, dried, and evaporated to a clear brown syrup (9 g.). This was refluxed for 4½ hours with a mixture of acetic acid (33 c.c.), hydrobromic acid of constant b. p. (22·5 c.c.), and water (13 c.c.), carbon dioxide being evolved. After evaporation under reduced pressure, the residue, in ether, was washed with 5% potassium carbonate solution; the ethereal layer yielded a brown resin, which was hydrolysed by being heated for 30 minutes at 100° with 2% sodium hydroxide solution. After being washed with ether, the aqueous layer was treated with charcoal and acidified, and the precipitate isolated with ether and distilled. *δ-(2-Bromo-5-methoxyphenyl)-δ-hydroxyvaleric acid*, b. p. 125—130° (bath temp.)/0·05 mm., set to pale-yellow needles (Found: C, 47·9; H, 5·0. $C_{12}H_{15}O_4Br$ requires C, 47·5; H, 5·0%).

α-(2-Bromo-5-methoxybenzylidene)glutaric Acid.—Sodium glutarate (13·5 g.), 2-bromo-5-methoxybenzaldehyde (16 g.), and acetic anhydride (110 c.c.) were heated for ten hours at 130—140°. Boiling water (300 c.c.) was added and then sufficient acetic acid to dissolve everything except a small amount of residual oil. The supernatant liquid was decanted and on cooling yielded the *benzylideneglutaric acid* (7·8 g.). The mother-liquors gave a further quantity (4·4 g.) of the acid. It separated from aqueous acetic acid in pale-yellow needles, m. p. 188—189° (Found: C, 47·1; H, 3·7. $C_{13}H_{13}O_5Br$ requires C, 47·4; H, 3·9%), $\lambda_{max.}$ 2750, 3300 A., $\varepsilon_{max.}$ 10,600, 2200 (in methanol). The substance rapidly decolorised permanganate solution.

δ-(2-Bromo-5-methoxyphenyl)-γ-carboxy-δ-valerolactone.—A solution of the above acid (0·5 g.) in 2N-sodium carbonate solution was acidified with an excess of dilute hydrochloric acid. After 6 days at room temperature, the *lactone* (0·4 g.) was collected. It crystallised from aqueous ethanol in colourless needles, m. p. 231—233° (Found: C, 47·0; H, 3·7. $C_{13}H_{13}O_5Br$ requires C, 47·4; H, 3·9%). The substance did not decolorise potassium permanganate solution.

Absorption spectra are by Dr. F. B. Strauss.

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38. *The Crystal Structures of the Acid Salts of Some Monobasic Acids. Part II. Potassium Hydrogen Di-p-hydroxybenzoate Hydrate.*

By J. M. SKINNER and J. C. SPEAKMAN.

The crystal structure of potassium hydrogen di-*p*-hydroxybenzoate hydrate, $KH(C_7H_5O_3)_2.H_2O$, has been elucidated by *X*-ray methods. The crystal can be regarded as having a layer structure. The carboxyl groups are arranged about the potassium ions and acidic hydrogen atoms, the latter taking part in short (and apparently symmetrical) hydrogen bonds, and the pattern here is very similar to that found in some other acid salts (*e.g.*, cf. Part I). The phenolic hydroxyl groups and water molecules are involved in a somewhat complex situation, including hydrogen bonds, some of which also appear to be symmetrical. In this region there is a difference between the number of available protons and the number of presumptive hydrogen bonds.

THE almost universal occurrence of acid salts of monocarboxylic acids was stressed in Part I (*J.*, 1949, 3357), which reported an analysis of the crystal structure of potassium hydrogen bisphenylacetate. The present paper describes a similar investigation of the corresponding di-*p*-hydroxybenzoate.

EXPERIMENTAL.

Preparation and Chemical Analysis.—Acid potassium salts (KHX_2), unlike the acid sodium salts, are generally not hydrated. Potassium hydrogen di-*p*-hydroxybenzoate was first described by Farmer (*J.*, 1903, **73**, 1440), and its formula given as $KH(C_7H_5O_3)_2$. In an attempt to prepare this compound, 6·2 g. of *p*-hydroxybenzoic acid monohydrate and 1·54 g. of potassium carbonate were heated in refluxing methylated spirit until no more carbon dioxide was evolved. The solid which appeared on cooling was recrystallised from alcohol. The equivalent, as first determined by titration with sodium hydroxide, bromophenol-blue being used as indicator, appeared to confirm Farmer's formula, although the end-point was not very sharp owing to the appreciable acidity of the phenolic group ($pK_1 = 4·6$, $pK_2 = 9·5$; cf. *J.*, 1944, 20). However, as the crystal analysis proceeded, it became clear that the compound was hydrated. The formula $KH(C_7H_5O_3)_2.H_2O$ was indicated by potassium estimation (Found: 11·6$_4$. Calc.: 11·7$_6$%), and confirmed by the density and *X*-ray data. The molecule of water appears to be firmly held, for no change of composition occurred after the crystals had been heated at 100° *in vacuo*. No evidence of an anhydrous salt was obtained; and it is noteworthy that, even if the anhydrous acid and dry solvent were used in the preparation, sufficient water to form the hydrate would be generated in the reaction. The anomaly presented by this hydration of an acid potassium salt is apparent only, since the water molecule proved to be associated with the phenolic hydroxyl groups, and not with the ionised groups.

Crystal Data.—The crystals consisted of thin laths, elongated in the direction of [*b*], and with the form {100} most prominent. They showed straight extinction between crossed Nicols. The following data

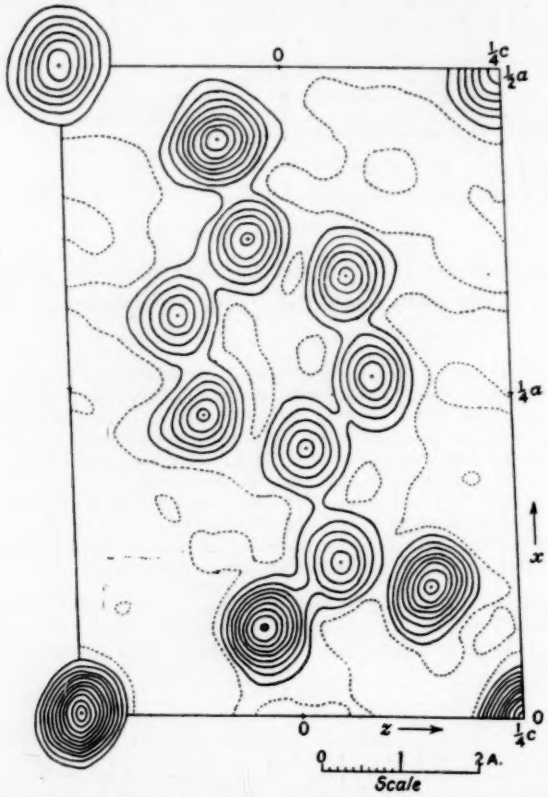
were established by single crystal rotation and oscillation photographs, using copper K-α radiation ($\lambda = 1{\cdot}54_8$ A.).

Potassium hydrogen di-*p*-hydroxybenzoate hydrate: $KH(C_7H_5O_3)_2,H_2O$; M, 332·3; appears to decompose >200°; monoclinic prismatic; $a = 16{\cdot}40$ (±0·05), $b = 3{\cdot}82$ (±0·02), $c = 11{\cdot}30$ (±0·03) A., $\beta = 92{\cdot}5°$ (±0·5°); volume of unit cell, 707 A.^{3}; d (calc.) 1·561, d (found) 1·54—1·55; two molecules per unit cell; $F(000)$ 344; absorption coefficient for X-rays ($\lambda = 1{\cdot}54_8$ A.), $\mu = 37$ cm.$^{-1}$.

Absent spectra: ($h0l$) when l is odd. Space group, $C_s^2 - Pc$, or $C_{2h}^4 - P2/c$. The latter was adopted and appears to be justified by the outcome; it implies that each stoicheiometric molecule possesses either a centre of symmetry or a two-fold axis.

FIG. 1.

Fourier synthesis (F_{h0l}) *for potassium hydrogen di-p-hydroxybenzoate hydrate, projected along* b*-axis. Contour-line scale: 1 electron per sq.* A.*; line of unit electron-density broken; alternate contours only are shown for the potassium ion.*



Experimental Methods and Details of Analysis.—Relative intensity measurements (covering a range of 1000 to 1) were made, and were placed upon an absolute scale, by the methods described in Part I. Some 260 spectra out of a theoretically accessible 402 were measured in the principal zones, $h0l$, $hk0$, and $0kl$, attention being concentrated mainly on the first two.

The similarities to the crystal data for potassium hydrogen bisphenylacetate, including the shortness of the *b*-axis, suggested that the molecules lay nearly parallel to the *xz*-plane, and that analysis could best start from the ($h0l$) spectra. A Patterson synthesis proved rather misleading; but a similar synthesis, using corresponding data for the isomorphous rubidium hydrogen di-*p*-hydroxybenzoate hydrate [for which $a = 16{\cdot}47$ (±0·04), $b = 3{\cdot}91$ (±0·02), $c = 11{\cdot}50$ (±0·03) A., $\beta \approx 93\frac{1}{2}°$] gave a useful projection. This led by successive Fourier syntheses to the final electron-density projection for the potassium salt shown in Fig. 1, and interpreted in Fig. 2. All the atoms (other than hydrogen) are well resolved, their x- and z-co-ordinates could be found, and the structural plan was proved to be very similar to that of the phenylacetate.

For reasons detailed in Part I, a centre of symmetry which was taken as origin must be assumed to lie between O(2) and O(2′), and the potassium ions must be assumed to lie on digonal axes. In consequence the water molecule [referred to as $H_2O(1)$] must lie on another set of digonal axes, and there must be a centre of symmetry between O(4) and O(4‴). The projected appearance of the benzene ring suggests that it is appreciably inclined to the *xz*-plane in the direction of C(3)–C(7), but hardly at all in that of C(2)–C(5). The apparent separation of K^+ and O(3) being only 2·0 A., there must be nearly the maximum difference ($\frac{1}{2}b$ = 1·9 A.) between the *y*-co-ordinates of these atoms if a normal K–O distance is to be maintained. These, and other similar, considerations led to a preliminary set of *y*-co-ordinates, which was refined mainly by trial-and-error methods. Some guidance was had from Fourier projections along [*z*], but these were not very helpful because of the low resolution in this direction and because only 4 orders of *h* were accessible. The set of co-ordinates given in Table I was ultimately adopted. Atomic positions are also shown with respect to orthogonal axes —[*x*′] and [*z*′], the latter being orientated parallel to [*z*]. The *x*- and *z*-co-ordinates, based on the excellent [*y*]-projection, are considered to be reliable to ±0·02 A.; for reasons implied above, the *y*-co-ordinates are less certain, the error being estimated at ±0·04 A.

FIG. 2.

Numbering and arrangement of atoms in b*-axis projection, based on Fig.* 1. (*The centres of symmetry shown on the lines* x = 0 *and* ½a *are at* y = 0 *and* ½b.)

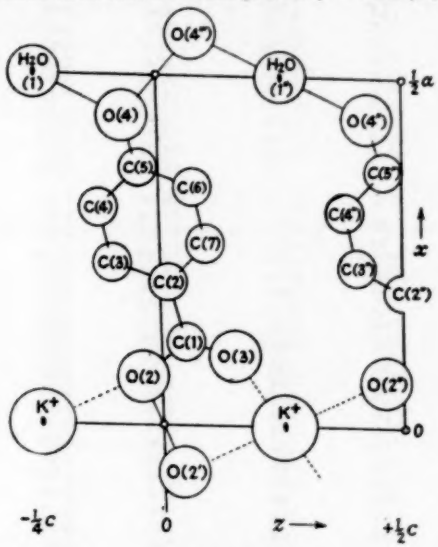


TABLE I.

Atomic co-ordinates.

(Origin at centre of symmetry. See Fig. 2 for numbering of atoms. *x*, *x*′, *y*, *z* and *z*′ *in* A.)

Atom.	*x*/*a*.	*x*.	*x*′.	*y*/*b*.	*y*.	*z*/*c*.	*z*.	*z*′.
K^+	0·0000	0·00	0·00	−0·333	$-1·27_9$	0·2500	$2·82_5$	$2·82_5$
$H_2O(1)$	0·5000	$8·20_0$	$8·19_5$	−0·017	$-0·06_4$	−0·2500	$-2·82_5$	$-3·18_7$
O(2)	0·0675	$1·10_8$	$1·10_6$	0·125	$0·47_8$	−0·0395	$-0·44_6$	$-0·49_5$
O(3)	0·0994	$1·63_0$	$1·62_6$	0·133	$0·50_0$	0·1509	$1·70_5$	$1·63_8$
O(4)	0·4432	$7·26_9$	$7·26_1$	0·350	$1·33_7$	−0·0728	$-0·82_3$	$-1·14_4$
C(1)	0·1191	$1·95_4$	$1·95_2$	0·150	$0·57_3$	0·0500	$0·56_5$	$0·47_6$
C(2)	0·2056	$3·37_1$	$3·36_8$	0·208	$0·79_4$	0·0149	$0·16_9$	$0·02_9$
C(3)	0·2309	$3·78_6$	$3·78_3$	0·133	$0·50_0$	−0·0982	$-1·11_0$	$-1·27_8$
C(4)	0·3080	$5·05_3$	$5·04_7$	0·167	$0·63_7$	−0·1246	$-1·40_8$	$-1·63_1$
C(5)	0·3661	$6·00_3$	$5·99_7$	0·308	$1·17_8$	−0·0412	$-0·46_6$	$-0·73_1$
C(6)	0·3389	$5·55_8$	$5·55_2$	0·383	$1·46_4$	0·0693	$0·78_3$	$0·53_7$
C(7)	0·2617	$4·29_2$	$4·28_8$	0·350	$1·33_7$	0·0939	$1·06_1$	$0·87_1$

Structure-factors calculated from these co-ordinates are given in Tables II and III. For carbon and oxygen the atomic scattering factors were those used in Part I, but a slightly different function was used for potassium:

sin θ	0·0	0·1	0·2	0·3	0·4	0·5	0·6	0·7	0·8	0·9
f_{K^+}	18·0	16·1	$13·3_8$	10·4	7·8	6·2	$5·0_4$	4·1	$3·1_5$	2·6

TABLE II.

Observed structure amplitudes and calculated structure factors for h0l.

h0l.	2 sin θ.	$F_{meas.}$	$F_{calc.}$	*h0l.*	2 sin θ.	$F_{meas.}$	$F_{calc.}$
200	0·19	18	+12	$\bar{8}04$	0·91	23	+26
300	0·28	22	+23	$\bar{7}04$	0·84	< 5	− 9
400	0·38	17	+17	$\bar{6}04$	0·77	27	+30
500	0·47	20	−25	$\bar{5}04$	0·71	< 5	0
600	0·56	7	−12	$\bar{4}04$	0·65	24	+26
700	0·66	22	−16	$\bar{3}04$	0·60	32	−37
800	0·75	9	+10	$\bar{2}04$	0·57	54	+44
900	0·85	45	+39	$\bar{1}04$	0·55	22	+14
10,00	0·94	12	+14	004	0·54	12	+11
11,00	1·03	18	+18	104	0·56	31	+27
12,00	1·13	12	+12	204	0·58	54	+48
13,00	1·22	6	+ 6	304	0·62	53	+49
14,00	1·32	13	+15	404	0·67	14	+17
15,00	1·41	4	+ 3	504	0·73	61	+63
16,00	1·50	18	+16	604	0·80	39	+37
17,00	1·60	3	0	704	0·87	8	− 6
18,00	1·69	7	+ 9	804	0·95	< 6	+ 4
19,00	1·79	6	+ 4	904	1·02	9	−13
20,00	1·87	8	+10	10,04	1·10	< 7	+ 3
21,00	1·97	4	− 2	11,04	1·19	< 7	− 1
				12,40	1·27	< 7	+ 3
$\bar{1}9,02$	1·80	8	− 6	13,04	1·35	13	− 7
$\bar{1}8,02$	1·70	7	−10	14,04	1·44	39	+37
$\bar{1}7,02$	1·61	10	+12	15,04	1·53	18	+14
$\bar{1}6,02$	1·52	< 7	+ 4				
$\bar{1}5,02$	1·43	< 7	+ 3	$\bar{1}8,06$	1·85	7	−10
$\bar{1}4,02$	1·34	13	−18	$\bar{1}7,06$	1·77	8	− 7
$\bar{1}3,02$	1·24	10	+10	$\bar{1}6,06$	1·69	11	−14
$\bar{1}2,02$	1·15	< 7	−16	$\bar{1}5,06$	1·60	10	− 7
$\bar{1}1,02$	1·06	< 5	+ 4	$\bar{1}4,06$	1·53	13	−12
$\bar{1}0,02$	0·97	32	−35	$\bar{1}3,06$	1·45	< 7	− 8
$\bar{9}02$	0·88	6	+ 3	$\bar{1}2,06$	1·37	23	−19
$\bar{8}02$	0·79	32	−43	$\bar{1}1,06$	1·29	7	+ 7
$\bar{7}02$	0·70	51	−61	$\bar{1}0,06$	1·22	32	+26
$\bar{6}02$	0·62	42	−55	$\bar{9}06$	1·15	21	−13
$\bar{5}02$	0·54	30	−34	$\bar{8}06$	1·09	20	−12
$\bar{4}02$	0·46	17	−21	$\bar{7}06$	1·03	19	−13
$\bar{3}02$	0·38	10	− 9	$\bar{6}06$	0·98	32	−24
$\bar{2}02$	0·33	< 3	− 3	$\bar{5}06$	0·92	31	−28
$\bar{1}02$	0·28	13	−16	$\bar{4}06$	0·88	42	−42
002	0·27	63	+65	$\bar{3}06$	0·85	50	−42
102	0·29	13	−16	$\bar{2}06$	0·83	16	−22
202	0·34	70	−90	$\bar{1}06$	0·82	21	+19
302	0·40	15	−13	006	0·82	40	−38
402	0·47	59	−66	106	0·83	13	+15
502	0·55	18	+22	206	0·84	10	−12
602	0·63	24	−31	306	0·87	10	+15
702	0·72	5	+ 1	406	0·91	17	−24
802	0·81	28	−29	506	0·95	< 6	+ 3
902	0·90	6	− 8	606	1·01	< 6	− 9
10,02	0·99	32	−30	706	1·07	20	−23
11,02	1·08	9	−13	806	1·13	20	−17
12,02	1·17	38	−38	906	1·19	10	−12
13,02	1·26	32	−26	10,06	1·27	10	−12
14,02	1·35	22	+13	11,06	1·34	13	−12
15,02	1·45	< 7	− 4	12,06	1·41	8	− 8
16,02	1·54	< 7	− 5	13,06	1·49	7	− 8
17,02	1·63	< 7	+ 3				
18,02	1·72	< 6	0	$\bar{1}4,08$	1·68	12	+11
19,02	1·81	< 6	− 3	$\bar{1}3,08$	1·60	12	+11
				$\bar{1}2,08$	1·54	13	+10
$\bar{1}6,04$	1·58	13	+15	$\bar{1}1,08$	1·47	13	+11
$\bar{1}5,04$	1·49	13	+15	$\bar{1}0,08$	1·41	39	+37
$\bar{1}4,04$	1·41	< 8	+ 3	$\bar{9}08$	1·35	< 7	− 4
$\bar{1}3,04$	1·32	13	+20	$\bar{8}08$	1·30	< 7	− 2
$\bar{1}2,04$	1·24	< 7	+ 7	$\bar{7}08$	1·25	< 7	+ 2
$\bar{1}1,04$	1·15	21	+14	$\bar{6}08$	1·21	< 7	+ 6
$\bar{1}0,04$	1·07	23	+22	$\bar{5}08$	1·16	10	+ 9
$\bar{9}04$	0·99	< 6	+ 4	$\bar{4}08$	1·14	12	+ 9
				$\bar{3}08$	1·11	10	+ 9

TABLE II—*continued.*

*h*0*l*.	2 sin θ.	$F_{meas.}$	$F_{calc.}$	*h*0*l*.	2 sin θ.	$F_{meas.}$	$F_{calc.}$
$\bar{2}08$	1·09	20	+13	$\bar{3}0,10$	1·37	13	− 8
$\bar{1}08$	1·09	20	+17	$\bar{2}0,10$	1·36	23	−22
008	1·08	11	+ 6	$\bar{1}0,10$	1·36	23	−18
108	1·09	12	+10	00,10	1·36	23	−20
208	1·11	10	− 7	10,10	1·36	8	− 8
308	1·14	< 6	+ 7	20,10	1·38	34	−25
408	1·16	36	+37	30,10	1·40	11	− 7
508	1·20	12	+ 6	40,10	1·42	28	+23
608	1·24	18	+24	50,10	1·45	8	− 2
708	1·29	10	+10	60,10	1·49	8	− 8
808	1·34	15	+20				
908	1·40	< 7	+ 7	$\bar{9}0,12$	1·80	8	+ 9
10,08	1·46	< 7	+ 9	$\bar{8}0,12$	1·76	15	+14
11,08	1·52	10	−10	$\bar{7}0,12$	1·73	9	+ 7
12,08	1·59	< 7	+ 5	$\bar{6}0,12$	1·70	7	+ 5
13,08	1·66	7	+ 7	$\bar{5}0,12$	1·68	7	+13
				$\bar{4}0,12$	1·66	7	+ 6
$\bar{1}1,0,10$	1·68	7	− 6	$\bar{3}0,12$	1·64	7	− 5
$\bar{1}0,0,10$	1·62	7	− 7	$\bar{2}0,12$	1·64	< 7	+ 2
$\bar{9}0,10$	1·57	7	− 7	$\bar{1}0,12$	1·63	< 7	− 2
$\bar{8}0,10$	1·53	7	− 9	00,12	1·63	< 7	+ 6
$\bar{7}0,10$	1·49	< 7	− 2	10,12	1·64	< 7	+ 3
$\bar{6}0,10$	1·45	11	−10	20,12	1·65	< 7	+10
$\bar{5}0,10$	1·42	11	+12	30,12	1·66	< 7	+ 3
$\bar{4}0,10$	1·39	8	−10	40,12	1·68	16	+21

TABLE III.

Observed structure amplitudes and calculated structure factors for hk0.

*hk*0.	2 sin θ.	$F_{meas.}$	$F_{calc.}$	*hk*0.	2 sin θ.	$F_{meas.}$	$F_{calc.}$
010	0·41	19	−25	15,20	1·62	3	− 4
110	0·42	33	+35	16,20	1·70	3	− 4
210	0·45	6	+ 3	17,20	1·79	2	− 2
310	0·49	33	−35	18,20	1·87	2	+ 2
410	0·55	4	−11	19,20	1·95	8	− 8
510	0·62	35	−42				
610	0·69	15	−20	030	1·22	7	+ 5
710	0·77	31	−33	130	1·22	< 2	−14
810	0·85	10	− 2	230	1·23	18	+16
910	0·93	14	−13	330	1·25	13	+12
10,10	1·02	18	+18	430	1·27	16	+16
11,10	1·11	19	−18	530	1·30	14	+16
12,10	1·19	6	− 3	630	1·34	8	+16
13,10	1·28	7	0	730	1·38	7	+13
14,10	1·37	< 2	− 2	830	1·43	10	+13
15,10	1·46	3	− 8	930	1·47	3	+ 2
16,10	1·55	< 2	− 1	10,30	1·53	7	− 6
17,10	1·64	5	+ 2	11,30	1·59	12	+15
18,10	1·73	< 2	− 2	12,30	1·65	11	+11
19,10	1·83	< 1	− 2	13,30	1·72	5	+ 1
20,10	1·92	6	− 6	14,30	1·79	10	+10
				15,30	1·86	6	+ 6
020	0·81	26	−25	16,30	1·93	6	+ 8
120	0·81	15	−11				
220	0·83	3	+ 6	040	1·62	9	−20
320	0·86	9	−11	140	1·62	< 2	− 7
420	0·89	5	+ 1	240	1·64	4	− 2
520	0·93	11	−14	340	1·65	5	− 6
620	0·99	5	+ 1	440	1·66	3	+ 2
720	1·04	11	− 8	540	1·68	< 2	− 4
820	1·10	10	+ 6	640	1·71	< 2	+ 7
920	1·16	18	−14	740	1·75	4	− 2
10,20	1·23	13	− 4	840	1·79	3	− 1
11,20	1·31	14	−10	940	1·83	5	−10
12,20	1·38	8	+ 4	10,40	1·87	3	+ 3
13,20	1·46	3	− 5	11,40	1·92	2	− 5
14,20	1·54	2	− 3	12,40	1·97	1	+ 4

The discrepancy for the 138 observed reflexions in the zone *h*0*l* is 17·9%, and that for the 82 in *hk*0 24·9%. (To dispose of certain ambiguities which would otherwise have arisen, a few structure factors were also worked out for 0*kl* and were in general agreement with the observed amplitudes.) The

percentage discrepancy figures are less good than those found in Part I. This can be attributed to the smaller number of strong reflexions. Indeed the average (absolute) discrepancies are $3{\cdot}0_4$ ($h0l$) and $2{\cdot}6_7$ ($hk0$), which compared reasonably well with the respective values, $5{\cdot}0_4$ and $4{\cdot}7_7$, for the doubly-primitive cell described in Part I. The agreement is judged to be adequate to sustain the proposed structure. The y-co-ordinates are liable to be more in error than the others.

Discussion.

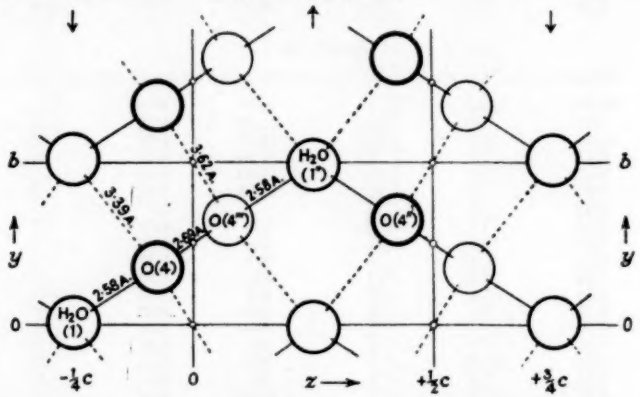
The crystal can be regarded as having a layer-structure parallel to (100), the elements of which are layers of (i) potassium ions and acidic hydrogen atoms (KH), (ii) *p*-hydroxybenzoate residues, and (iii) water molecules, arranged in the sequence :

$$(KH)\ (O_2C{\cdot}C_6H_4{\cdot}OH)\ (H_2O)\ (HO{\cdot}C_6H_4{\cdot}CO_2)\ (KH)\ \ldots$$

Immediately to either side of layer (i) the structure closely resembles that of the phenyl-acetate. Each potassium ion is surrounded by six, approximately equidistant (2·7—3·1 A.), oxygen atoms. These lie at the corners of a considerably distorted octahedron. The distortion may be attributed to hydrogen bonding, and it leaves a channel along which the potassium ion might be able to vibrate with relative ease. It is in this direction that the electron-density peak is elongated.

Fig. 3.

Arrangement of water molecules and phenolic hydroxyls in or near the plane $x = \frac{1}{8}a$. *The former* [$H_2O(1)$] *lie in this plane ; the latter* [O(4)] *are on the nearer side of this plane when represented by heavier circles, and on the further side when represented by fainter.*



The acidic hydrogen must be presumed to lie between O(2) and O(2′), which are thus joined by a short (2·61 A.) hydrogen bond. Its length is not known very accurately, owing to the uncertainty in the y-parameters; but all other structures examined, which involved lengthening this bond, impaired the agreement between observed and calculated structure amplitudes. This is a third instance (*Nature*, 1948, **162**, 695; Brown, Peiser, and Turner-Jones, *Acta Crystall.*, 1949, **2**, 174) of an apparently symmetrical hydrogen bond, and the comments in Part I (p. 3363) are relevant.

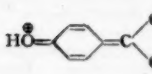
The situation between the hydroxyl groups [O(4)] and the water molecules [$H_2O(1)$] is somewhat similar, though considerably more complex (see Fig. 3). O(4) and O(4′′′) are 2·69 A. apart, which corresponds to a short bond; and, as these atoms are related by a centre of symmetry, the bond is symmetrical, at least in a statistical sense. The other hydrogen bonds, which must be presumed to occur in this region and are indicated by continuous lines in Fig. 3, are not required to be symmetrical. There is, however, the further complication of a difference between the numbers of available protons and of presumptive hydrogen bonds. If only the " short " inter-oxygen distances are counted (continuous lines in Fig. 3), there are 6 such bonds per unit cell, and 8 protons; and if, on the other hand, hydrogen bonds are also supposed to exist corresponding to the longer distances (broken lines), then there would be 12 bonds in all. In neither case can a single structure be written so as to conform to the crystal symmetry. The explanation offered is that there is ease of proton rearrangement, so that a statistical symmetry

is satisfied. If this be the true explanation, marked entropy (and other related) effects might be detectable (*e.g.*, cf. Ubbelohde, *J. Chim. physique*, 1949, **46**, 429; cf. also, *Ann. Reports*, 1949, **46**, 21).

TABLE IV.

Principal interatomic distances (A.).

Atoms.	Distance.	Atoms.	Distance.	Atoms.	Distance.
O(2)–O(3)	2·19	C(4)–C(5)	1·37	O(2)–O(2′)	2·61
C(1)–O(2)	1·29	C(5)–C(6)	1·37	O(4)–O(4″)	2·69
C(1)–O(3)	1·20	C(6)–C(7)	1·31	K^+–O(2)	3·10
C(1)–C(2)	1·50	C(7)–C(2)	1·37	K^+–O(3)	2·70
C(2)–C(3)	1·39	C(5)–O(4)	1·34		
C(3)–C(4)	1·32	H_2O(1)–O(4)	2·58	Angle O(2)–C(1)–O(3)	123°



Some of the bond-lengths in the *p*-hydroxybenzoate residue appear to be anomalous (Table IV), and by amounts probably exceeding experimental error (*ca.* ±0·04 A.). They are in the sense that suggests some degree of resonance with the "quinonoid" form (inset). The benzene ring is planar within the limits indicated.

In general the structure appears to be a fairly open one, with nearly all intermolecular distances exceeding 4·0 A. There are three exceptions: C(4) and C(7) of adjacent molecules are 3·72 A. apart; C(4) and H_2O(1) 3·55; and C(6) and O(1″) 3·61 A.

The authors thank the Department of Scientific and Industrial Research for grants which enabled one of them (J. M. S.) to take part in this work.

THE UNIVERSITY, GLASGOW, W.2. [*Received, August 23rd*, 1950.]

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39. *Some Physical Properties Associated with "Aromatic" Electrons. Part III. The Pseudo-metallic Properties of Potassium–Graphite and Graphite–Bromine.*

By F. R. M. MCDONNELL, R. C. PINK, and A. R. UBBELOHDE.

Graphite is known to form "lamellar compounds" C_8K and C_8Br by absorption of potassium and bromine, respectively. Physical properties of these compounds have been studied to elucidate the nature of the bonding, and its effects on the aromatic π electrons in graphite.

The marked diamagnetism associated with the π electrons in graphite is destroyed in both compounds. C_8Br is weakly diamagnetic, and C_8K shows a temperature-independent paramagnetism of the same order as for metallic calcium. Both compounds are better conductors of electricity than is graphite.

A tentative interpretation of these effects is given in the light of the band theory of the energy levels in graphite. The layers of fused aromatic nuclei are regarded as amphoteric, and can both take up electrons from the potassium atoms, and give them up to the bromine atoms, yielding pseudo-metallic structures in both cases.

Magnetic and electrical data on a compound of formula C_4F whose structure has not yet been established by other means suggest a general similarity in behaviour with graphite.

IN Parts I and II (Pink and Ubbelohde, *Trans. Faraday Soc.*, 1948, **44**, 708; McDonnell, Pink, and Ubbelohde, *ibid.*, 1950, **46**, 156), the possibility of resonance coupling of "aromatic" electrons in *cyclo*octatetraene was studied by means of the magnetic susceptibility and its temperature coefficient. With graphite, in addition to the magnetic susceptibility, other physical properties such as the electrical conductance can give important information about the π electrons. The present investigation was carried out to determine how far these electrons are affected by the formation of "lamellar compounds" in which foreign atoms or groups are intercalated between the layers of fused aromatic nuclei. For reasons of simplicity, the "compounds" C_8K and C_8Br were studied in the first instance. A substance of unknown

structure with the empirical formula C_4F which was made available by Imperial Chemical Industries Limited was included, since it seemed likely to show related behaviour.

As is detailed below, the main result of these investigations is to show that the π electrons are very markedly affected by the intercalated atoms. The behaviour of both C_8K and C_8Br is actually closer to that of " good " metals than that the parent graphite. The properties of C_4F suggest a different mode of binding of fluorine from the binding of potassium or bromine with the graphite.

Experimental.

Graphite was available in a wide variety of samples, both polycrystalline and in the form of crystals of 1 mm. or more edge, from natural sources, and from " Kish," kindly supplied by B.I.S.R.A. However, work on single crystals did not seem profitable owing to the break-up which takes place on forming the lamellar compounds. The bulk of the work was therefore carried out on a sample of polycrystalline graphite specially freed from paramagnetic ions, and of high purity, kindly supplied by A.E.R.E. Its analysis showed :

Ash, 0·09%. Specific impurities, in p.p.m. : Ca 300, Va 130, Si 130, Fe 40, Ti 25. Less than 5 p.p.m. : B, Cd, Li, Mg, Mn, Pb, Sn, W, Mo, Ni, Bi, Be, Co, Ag, Zn, Sb, As, Cr, Al, Ba, Sr, In, Sc, Y, La, Ce, Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Yb, Lu.

Inspection of Debye–Scherrer *X*-ray diagrams with stationary specimens showed that the crystallites gave reflections with (*hki*0) sharp, (000*l*) rather diffuse, and (*hkil*) with *l* large, very diffuse. Thus the lamellar spacings appear to be well defined. The extension of the layers and the accuracy of orientation about the *c* axis do not extend beyond about 10^{-5} cm.

Samples of graphite used for susceptibility measurements were degassed *in vacuo* for 2 hours at 500° before being transferred *in vacuo* to a previously calibrated Gouy tube.

Potassium–Graphite.—Potassium metal (B.D.H.) was used as a starting material. Before use it was filtered from oxide and distilled twice in a Pyrex vessel. These distillations were conducted at a low temperature to prevent the formation of the paramagnetic yellow peroxide KO_2 (Neuman, *J. Chem. Physics*, 1934, **2**, 31). The final material was shown by measurements at different field strengths to be free from ferro-magnetic impurites; m. p. (cooling curve) 63·4° (I.C.T. give 62·3°).

Potassium–graphite was prepared by the method of Fredenhagen and Suck (*Z. anorg. Chem.*, 1929, **178**, 353), which ensures that contact between the potassium and the graphite occurs only through the vapour phase. In the early experiments the major difficulty encountered in this preparation was the formation of a brown substance, probably KO_3, resulting from the attack of potassium on the Pyrex walls of the vessel during the prolonged periods of heating required. The quantity of this substance formed was sufficient in some instances to cause flakes of it to peel off the walls of the apparatus. Since the possibility of the admixture of KO_3 with the potassium–graphite could not be tolerated, in view of its highly paramagnetic nature, the whole of the apparatus was finally constructed from a special glass resistant to alkali metals, supplied by the General Electric Company, Limited. This glass (specification X4/NA/10), showed only very slight discoloration after 24 hours' exposure to potassium vapour at 400°. The potassium–graphite was transferred *in vacuo* to a previously calibrated Gouy tube, which was then sealed off.

The composition of the samples was determined from a knowledge of (i) the initial weight of graphite, (ii) the weight of potassium–graphite plus the ampoule in which it was first sealed off, and (iii) the weight of the ampoule determined subsequently by weighing it empty after transfer of the contents to the Gouy tube, together with the collected fragments of glass. The composition of different samples varied within the limits $KC_{8\cdot47-7\cdot79}$. The potassium-rich specimens may have contained some free potassium. Special precautions were used to carry out all measurements on potassium–graphite in high vacuum, since this compound rapidly autoxidises in air and since KO_2 is paramagnetic.

Preparation of Graphite–Bromine.—Graphite–bromine was prepared by keeping graphite over bromine in a sealed vessel for 24 hours (Thiele, *Z. anorg. Chem.*, 1932, **207**, 340; Rudorff, *ibid.*, 1941, **245**, 383). It was then quickly transferred to another vessel, which was cooled in liquid air, evacuated for some time, and then transferred to ampoules for sealing-off or to a previously calibrated Gouy tube as required. In this process some bromine was invariably lost. The actual composition of the samples of graphite–bromine on which measurements were made was determined as in the case of C_8K from a knowledge of (i) the weight of graphite, (ii) the weight of graphite–bromine plus ampoule, and (iii) the weight of the recovered ampoule.

" AnalaR " Bromine was used without further purification in the preparation of graphite–bromine. Its susceptibility was $-0\cdot337 \times 10^{-6}$ as compared with reported value of $-0\cdot39 \times 10^{-6}$ (I.C.T.).

The " tetracarbon fluoride " contained a ferromagnetic impurity, probably Fe_2O_3, which was removed by extraction (Soxhlet) with hot concentrated hydrochloric acid for 4 hours, after which it was washed free from chloride and dried. Even after this treatment it retained a temperature-dependent paramagnetism probably due to impurity (cf. Table I).

Bulk Densities.—For purposes of comparison with other data, the bulk densities of the various compounds were determined in the different conditions used for the resistivity and magnetic measurements. The data are recorded in Tables I and II.

Magnetic Measurements.—Susceptibility measurements were made by the Gouy method in the apparatus already described (McDonnell, Pink and Ubbelohde, *loc. cit.*). The only new feature was the use of a calibrated resistance and a microvolt potentiometer to measure the current through the magnet coils more accurately (to $\pm 0\cdot02\%$) than could be done with a calibrated ammeter. For the determination

TABLE I.

Magnetic susceptibilities (c.g.s. × 10^{-6}).

Substance.	90° K.: χ_v.	90° K.: χ_m.†	195° K.: χ_v.	195° K.: χ_m.†	288° K.: χ_v.	288° K.: χ_m.†	Bulk density in Gouy tube, g./c.c.
Potassium	+0·540	+21·1	+0·538	+21·0	+0·539	+21·1	0·849
Graphite (A.E.R.E.)	−7·909	−94·81	−6·757	−81·08	−6·04	−72·48	0·783
$KC_{8\cdot47}$	+1·01	+16·78	+1·01	+16·78	+1·00	+16·61	0·730
$KC_{7\cdot79}$	+0·953	+16·23	+0·951	+16·17	+0·953	+16·23	0·713
$BrC_{9\cdot98}$	−0·411	−8·23	−0·399	−7·99	−0·403	−8·07	0·979
C_4F *	−0·503 −0·538	−8·43 −9·03	−0·523	−8·76 −9·05	−0·527 −0·538	−8·83 −9·03	0·860
Bromine	—	—	—	—	−0·337	−26·96	3·13

* C_4F contained a temperature-dependent paramagnetic component (see above). The lower set of data has been corrected on the assumption that the paramagnetism is due to an impurity obeying the Weiss–Curie law.

† For graphite and its compounds χ_m has been calculated per g.-atom of carbon, to permit ready illustration of any effect on the electrons.

FIG. 1.

Apparatus for measurement of resistance of various lengths of compressed graphite and its compounds.

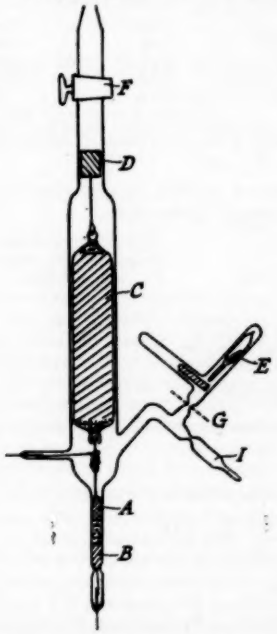
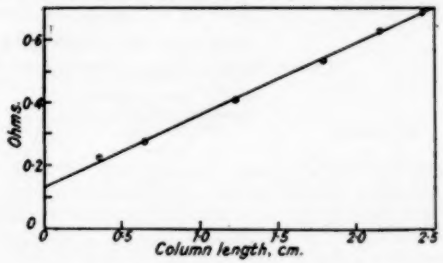


FIG. 2.

Resistance of columns of compressed graphite.



of the temperature coefficients of susceptibility measurements were in each case made at 90° K., 195° K., and 288° K. The Gouy tubes were calibrated with boiled-out distilled water, the specific susceptibility of which was taken to be $-0{\cdot}720 \times 10^{-6}$ c.g.s. units. Field strengths used were approximately 3700 and 2100 gauss. Except where otherwise stated, susceptibilities were found to be independent of field strength. Magnetic data are recorded in Table I.

Electrical Conductance and Thermoelectric Measurements.—The conductances were measured in the apparatus shown in Fig. 1, which permitted measurements to be made at a constant compression of 20·3 kg./cm.^{2} in a high vacuum. The two electrodes *A* and *B* are of brass; *B* is a close-sliding fit in the glass tubing and is held firmly in position with picein wax; *A* is a loose-sliding fit. Connection is made to the bridge through the two tungsten seals. The lead weight *C* for compression of the powdered

solids is encased in glass and has a mass of ~2 kg. *D* is a piece of soft iron which allows the upper electrode *A* to be held outside the electrode chamber magnetically while the substance under investigation is being added. The sample whose conductance is to be measured is contained originally in a sealed ampoule in *E*. When the apparatus has been evacuated, *F* is closed, the tip of the ampoule is broken off by allowing the weight to drop on the ampoule tip, and the sample shaken into the chamber *I*. A seal is then made at *G*. The substance is finally transferred to the electrode chamber in portions, a series of resistance measurements being made for columns of powder of heights ranging between 0·2 and 3·0 cm. Column heights were measured to $\pm$0·002 cm. with a travelling microscope. Corrections for leads and contact resistances were obviated by calculating the specific conductance from a knowledge of the cross-sectional area of the electrode chamber (0·118 sq. cm.), and the gradient of the plot of resistance against length of column. The data for graphite are shown in Fig. 2. The extrapolated curve does not pass through the origin, owing to the contact resistances at the brass electrodes. Conductance data calculated in this way are shown in Table II.

The same apparatus without modification was used for measurement of the thermoelectric E.M.F.'s. In these measurements a 3-cm. column of powdered solid was used, of which 1 cm. was immersed in liquid air. Owing to the short length of column which had to be used, it is unlikely that the hot junction fully attained the room temperature, but the signs and magnitudes of the effects recorded in Table III are comparative.

TABLE II.

Conductances of graphite and its compounds.

Substance.	Bulk density, g./c.c.	Conductance (ohm^{-1} $cm.^{-1}$). 90° K.	288° K.	Substance.	Bulk density, g./c.c.	Conductance (ohm^{-1} $cm.^{-1}$). 90° K.	288° K.
Kish	1·90	110	128	C_4F after heating *in vacuo* for 12 hrs. at 500°	0·968	—	17·0
Graphite (A.E.R.E.)	1·19	26·5	35·2	$BrC_{10\cdot5}$	1·41	—	223
$KC_{8\cdot47}$	—	—	1462	$BrC_{9\cdot9}$	1·92	197	384
$KC_{8\cdot46}$	—	1302	980	Metallic K (compact)	0·86	—	150,000
$KC_{8\cdot46}$	1·40	—	1271	Powdered Cu	2·15	—	850
$KC_{12\cdot2}$	—	1073	870	Compact Cu	8·3—8·9	—	580,000
$KC_{27\cdot6}$	1·05	—	565				
C_4F	1·03	0·222	0·389				

Note: The crystal density of graphite is 2·26 g./c.c. (Hoffmann, Wilm and Caslan, *Z. Elektrochem.*, 1936, **42**, 504).

TABLE III.

Thermo-electric voltage of graphite and its compounds against brass.

Substance.	E.M.F. (mv.) against brass, showing sign of "hot" junction.	Substance.	E.M.F. (mv.) against brass, showing sign of hot junction.
Kish	−0·5	$BrC_{9\cdot9}$ *	−2·4
Graphite (A.E.R.E.)	−1·4	C_4F	−1·5
$KC_{8\cdot47}$	+2·0	C_4F after heating for 12 hrs. *in vacuo* at 500°	−2·5
$KC_{12\cdot2}$	+2·2		
$KC_{27\cdot6}$	+2·4		

* Thin platinum foil over the brass electrodes.

In all the measurements with graphite–bromine the tips of the brass electrodes were protected with thin platinum foil.

DISCUSSION.

The broad general conclusion which emerges from the examination of the data in Table I—III is that graphite actually becomes "more metallic" on forming C_8K or C_8Br. The marked diamagnetism associated with the giant π orbitals is destroyed, and the electrical conductance is increased. These observations can be tentatively interpreted on the basis of a model in which the layers of graphite behave amphoterically, and take up electrons from the potassium, or give up electrons to the bromine. The bonds between the K or Br atoms and the graphite layers are probably "metallic" in nature. As in other inter-metallic compounds a range of compositions around the stoicheiometric value has approximately the same stability. Various aspects of this suggestion may be examined as follows.

(i) *Bond distances and bond energies of the lamellar compounds.* *X*-Ray-diffraction measurements show that the interlamellar distance of 3·35 A. in graphite increases to 7·76 A. when potassium forms C_8K and to 7·05 A. when bromine forms C_8Br (Schleede and Wellman, *Z. physikal. Chem.*, 1932, **18**, *B*, 1; Rudorff, *loc. cit.*). If the ions K^+ (radius 1·33 A.) and Br^- (radius 1·95 A.), respectively, were packed into layer ionic lattices, with the amphoteric layers of carbon atoms carrying charges of opposite sign, this should give the smaller spacing for the potassium layer lattice, contrary to what is observed. But if the potassium and bromine

atoms form essentially pseudo-metallic linkages with the layers of carbon atoms, the larger spacing required by potassium (metallic radius 2·23 A.) than by bromine (covalent singly-bonded radius 1·19 A.) is less difficult to understand.

The absorption of bromine as molecules (one of the hypotheses quoted by Rudorff, *loc. cit.*) does not explain the smaller space requirements compared with the potassium compound. [When our experiments were completed Goldsmith (*J. Chem. Physics*, 1950, **18**, 523) published magnetic studies on graphite–bromine on the basis of which he also postulated mainly intercalated bromine molecules.] Magnetic properties are further discussed below. A further objection to the assumption of absorbed bromine molecules is that this does not explain the effect of bromine on the conductance, and the concurrence in behaviour between bromine and potassium.

Complete energy data for the formation of the compounds are not available, but some data are available (Bichowsky and Rossini, "Thermochemistry of Chemical Substances," Reinhold, 1936, except where otherwise stated).

$$K_{gas} \longrightarrow K^+_{gas} + e;\ \Delta H_1 = +101{\cdot}1 \text{ kcals. mole}^{-1} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

These electrons fill the empty band in graphite (Wallace, *Physical Rev.*, 1947, **71**, 622; Coulson, *Nature*, 1947, **159**, 265) starting from a zero ground level which may conveniently be written as

$$e + [C_{lam.}] \longrightarrow [C^-_{lam.}];\ \text{(approx. thermoneutral)} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The K^+ ions are then intercalated by virtue of the electrostatic charges on the lamallæ:

$$K^+_{gas} + [C^-_{lam.}] \longrightarrow C_8K + \Delta H_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Addition of (1), (2), and (3) gives for the overall process

$$K_{gas} + [C_{lam.}] \longrightarrow C_8K;\ \Delta H = \Delta H_3 + 101{\cdot}1$$

From the data of Fredenhagen and Cadenbach (*Z. anorg. Chem.*, 1926, **158**, 249)

$$K_{liq.} + [C_{lam.}] \longrightarrow C_4K_{(excess\ K)};\ \Delta H = -6{\cdot}0$$

If the value for C_8K is taken to be of the same order, this would make

$$K_{liq.} + [C_{lam.}] \longrightarrow C_8K;\ \Delta H = -6{\cdot}0$$

or

$$K_{gas} + [C_{lam.}] \longrightarrow C_8K;\ \Delta H = -25{\cdot}2$$

so that $\Delta H_3 \approx -126$ kcals./mole.

This large energy evolution compensates for the ionisation energy of the potassium. Absorption of vapour proceeds readily when the vapour pressure of the potassium is ~0·005 atm. It is noteworthy that for sodium, where the ionisation energy is larger ($\Delta H_1 = +119{\cdot}5$ kcals./mole), the energy evolved on intercalation of Na appears to be insufficient to compensate the higher ionisation energy, since no lamellar compounds of graphite and sodium are known, whereas rubidium and cæsium, which have lower ionisation energies than potassium, both form lamellar compounds (Riley, *Fuel in Science and Practice*, 1945, **24**, 1). The non-intercalation of other metal atoms such as cadmium can probably be explained on similar lines.

For the bromine compound the net energy requirement of the process

$$\tfrac{1}{2}Br_{2\,gas} + e \longrightarrow Br^-_{gas};\ \Delta H_1 = -54 \text{ kcals. mole}^{-1} \quad . \quad . \quad . \quad . \quad (4)$$

strongly favours intercalation of the Br in the process

$$Br^-_{gas} + [C^+_{lam.}] \longrightarrow C_8Br;\ \Delta H_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

ΔH_3 might be expected to be lower than ΔH_3 owing to the larger size of Br^- than of K^+, but since the ultimate lamellar compounds probably involve inter-metallic rather than ionic bonds the calculation will not be pursued further. It need only be said that known energy data accord very reasonably with the pseudo-metallic model for potassium–graphite and graphite–bromine.

The ready wetting of C_8K or C_4K by excess of potassium (Fredenhagen and Cadenbach, *loc. cit.*, and present observations) indicates metallic bonding at the surface of separation of these two phases (cf. Ubbelohde, *J.*, 1950, 1143) and supports the general interpretation of metallic binding in these lamellar compounds.

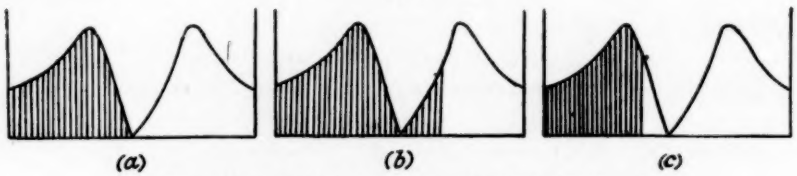
The correspondence between the bromine and the potassium compounds though not

complete is not unexpected, on the above basis, though further energy data are clearly required to complete the interpretation.

(ii) *Electrical conductivity of the compounds.* Experiments on single crystals of graphite indicate that $\sigma\perp$ is only a small fraction of the order of 10^{-4} of $\sigma=$, where $\sigma\perp$ is the conductance in a direction perpendicular and $\sigma=$ that parallel to the lamellæ. Unfortunately, the swelling and crumbling of single crystals when the lamellar compounds are formed necessitates the use of polycrystalline powders and precludes verification of whether the conductivity is equally affected in both directions by forming the lamellar compounds. A further difficulty arises with the polycrystalline powder in the interpretation of the changed sign of the temperature coefficient of conductance on compound formation. Polycrystalline graphite has a positive temperature coefficient of conductance, as has also " tetracarbon fluoride " and graphite–bromine; but C_8K has the negative temperature coefficient of conductance corresponding with a metal.

According to Wallace (*loc. cit.*), $\sigma=$ should have a negative temperature coefficient for a single crystal, and the positive temperature coefficient of polycrystalline graphite arises from the effect of temperature on the resistance *between* crystallites. However this may be, the marked increase in conductance observed in our experiments does seem to be most readily interpreted in terms of the part-filling of the empty electron band, in C_8K, and the part-emptying of the full electron band in C_8Br as sketched in Fig. 3. When the bromine or potassium is removed, the conductance falls again, so that the effects recorded in Table II can hardly be due to the influence of bromine or potassium on the " impurity atoms " at the edges of crystallites.

FIG. 3.



a. Electron energy levels in graphite according to Coulson (loc. cit.).
b. Suggested electron bands in potassium–graphite.
c. Suggested electron bands in graphite–bromine.
(*All at* 0° K.)

From the bulk densities, the carbon content per c.c. in the conductance experiments can be calculated as: in graphite, 0·099; in $KC_{5\cdot46}$, 0·084; in $KC_{22\cdot8}$, 0·079; in $BrC_{9\cdot9}$, 0·092 g.-atom. The increase in conductance on formation of graphite–bromine or potassium–graphite is clearly not due to a closer packing of the crystallites in the compressed powders. It is noteworthy that the conductance of powdered Cu (Table II) is of the same order as for potassium–graphite.

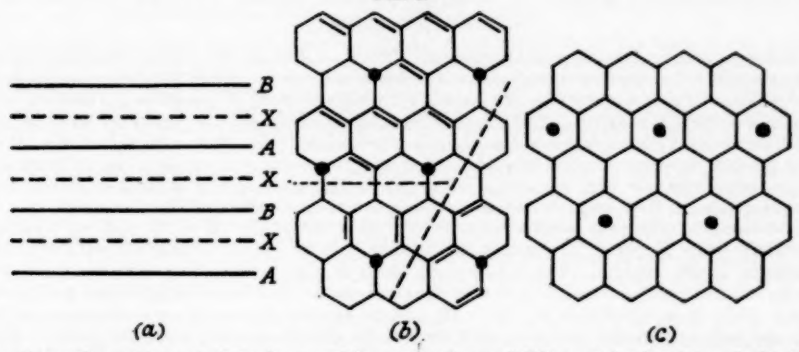
The change in colour in C_8K, which is a fine brown, and in C_8Br, which is steel-blue, likewise indicates that the effect of potassium or bromine is primarily on the energy levels of electrons within each crystallite. On the pseudo-metallic model suggested above for these compounds $\sigma\perp$ should show considerable increase on compound formation, but it has not yet been possible to test this. The change in magnitude and sign of the thermoelectric power against brass on compound formation gives further support to the above interpretation, since both compounds should resemble " better " metals, *i.e.*, with less completely filled energy levels than graphite.

(iii) *Magnetic data.* At present perhaps the most complete evidence about the bonding in these compounds is obtainable from the magnetic data, since here the problem of the contribution of inter-crystallite electron transitions does not arise. The weak temperature-independent diamagnetism of C_8Br is comparable with that of metals such as tin or zirconium and the comparatively strong temperature-independent paramagnetism of C_8K is comparable with that of metallic calcium. Both these are consistent with the picture obtained from the conductivity and thermoelectric data. It is noteworthy that compound formation leads to a pseudo-metal C_8K considerably more paramagnetic than pure solid potassium itself. That the electrons of the potassium must be used in bonding may be confirmed from the fact that isolated potassium atoms with unperturbed electron orbits would give a temperature-dependent magnetism which in C_8K would give χ_A $+27{\cdot}0 \times 10^{-6}$ at 90° K. and χ_A $+8{\cdot}4 \times 10^{-6}$ at 288° K.,

i.e., much larger than, and with quite a different temperature coefficient from, the observed values. A possible dependence of the susceptibility on field strength in the sense required by ferromagnetism was observed for C_8K. So far as observed it does not exceed 1% and is under further investigation.

(iv) *Structural relationships of the atoms in* C_8K *and* C_8Br. C_8K has been subjected to *X*-ray powder analysis (see refs. by Riley, *loc. cit.*). Though the interpretation is not unique, a plausible structure appears to be as indicated in Fig. 4. [The structure of C_8Br (Rudorff, *loc. cit.*) though probably related to C_8K is doubtful and is not reproduced here.]

FIG. 4.



a. Layer-plane sequence in potassium–graphite : carbon layers, full line ; potassium layers, broken line.
b. Position of carbon layer plane A with respect to potassium ion in X, showing three possible Kekulé-bond arrangements.
c. Position of carbon layer plane B with respect to potassium ions in X.

In the preceding sections an interpretation was developed according to which the intercalated potassium and bromine atoms form metallic bonds by releasing or taking electrons from the graphite. According to an alternative description a metallic system consists of covalent bonded atoms in electron-defect resonance. With this formulation K–C bonds might be illustrated as in Fig. 4, *a*—*c*. For a given location of potassium atoms three Kekulé-bond arrangements can be described. Each of these " canonical structures " leaves one electron per potassium atom with unpaired spin. At this stage the bond model does not appear to warrant further elaboration. It does, however, give a ready explanation of the ordered arrangement of potassium (and probably bromine) in the layers, since these atoms assume definite bonding locations in the pseudo-metallic system in resonance. Less favourable Kekulé resonance structures would be formed if a disordered arrangement of the intercalated atoms were taken up.

The authors thank Imperial Chemical Industries Limited for the gift of certain chemicals and for the loan of a microbalance, and A.E.R.E. for the graphite.

QUEEN'S UNIVERSITY, BELFAST. [*Received, August 30th*, 1950.]

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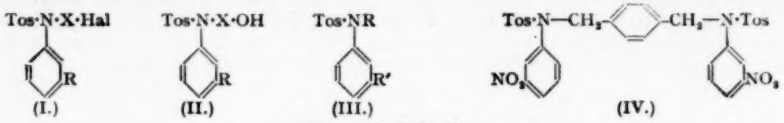
40. *The Preparation of Some Toluene-p-sulphonanilide Derivatives. A Note on the Reactivity of Ethylene Chlorohydrin.*

By J. GLAZER and E. E. TURNER.

The preparation of some *N*-alkyl- and *N*-ω-halogenoalkyl-toluene-*p*-sulphonanilides is described. It is suggested that the low reactivity of ethylene chlorohydrin towards the toluene-*p*-sulphonanilide ion ($\overset{\ominus}{N}R_2$) is due to intramolecular hydrogen bonding.

THE preparation and optical activation of *N*-benzenesulphonyl-*N*-2-hydroxyethyl-8-nitro-1-naphthylamine has recently been reported by Glazer, Harris, and Turner (*J.*, 1950, 1753). In

connection with the synthesis of this compound, the reactivity of toluene-*p*-sulphonanilide and toluene-*p*-sulphon-*m*-nitroanilide towards various halogeno-compounds became of interest: it was hoped to hydrolyse *N*-ω-halogenoalkylsulphonanilides (I) to the corresponding alcohols (II). In no case, however, did the hydrolysis succeed.



(I.) (II.) (III.) (IV.)

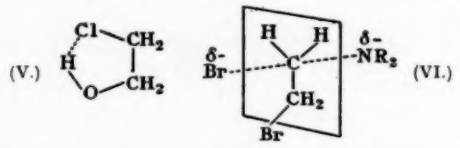
(Tos = *p*-$C_6H_4Me{\cdot}SO_2$)

N-Benzyltoluene-*p*-sulphon-*m*-nitroanilide (III; R = Ph·CH_2, R′ = NO_2) was obtained by boiling under reflux the sodium salt of toluene-*p*-sulphon-*m*-nitroanilide with benzyl chloride in dry ethanol. Its structure was confirmed by synthesis from *N*-benzyl-*m*-nitroaniline and toluene-*p*-sulphonyl chloride. The ease of this reaction suggested the possibility of obtaining *N*-*p*-hydroxymethylbenzyltoluene-*p*-sulphon-*m*-nitroanilide (II; X = ·CH_2·C_6H_4·CH_2·, R = NO_2) through the corresponding bromide. However, treatment of the sodium salt of toluene-*p*-sulphon-*m*-nitroanilide with *p*-xylylene dibromide in dry methanol or ethanol or in ethanol–acetone yielded *NN′*-*p*-xylylenebis(toluene-*p*-sulphon-*m*-nitroanilide) (IV).

N-2-Bromoethyltoluene-*p*-sulphonanilide (I; X = ·CH_2·CH_2·, R = H) and its *m*-nitro-derivative were prepared by heating the sodium salt of the sulphonanilide with ethylene dibromide in dry ethanol. The deactivating effect of the *m*-nitro-group was shown by the greater time of reaction needed to obtain the same yield. *N*-2-Methylallyltoluene-*p*-sulphonanilide (III; R = ·CH_2·$CMe{:}CH_2$, R′ = H) and its *m*-nitro-derivative were obtained by the same method, the greater reactivity of 2-methylallyl chloride leading to higher yields. Here again, the *m*-nitro-group markedly reduced the yield. Catalytic hydrogenation of the methylallyl compounds gave the corresponding *N*-*iso*butyl compounds in good yield.

Direct synthesis of *N*-2-hydroxyethyltoluene-*p*-sulphonanilide (II; X = ·CH_2·CH_2·, R = H) failed under a variety of conditions, but the nitro-derivative (II; X = ·CH_2·CH_2·, R = NO_2) was finally obtained by heating the sulphonanilide with ethylene chlorohydrin in alcoholic potassium hydroxide for six hours at 135°.

The lower reactivity of ethylene chlorohydrin and iodohydrin, compared with ethylene dibromide, towards attack by the sulphonanilide anion ($\overset{\ominus}{N}R_2$) is possibly caused by intramolecular hydrogen bonding, giving rise to a 5-membered ring (V). Zumwalt and Badger (*J. Amer. Chem. Soc.*, 1940, **62**, 305) concluded, from an infra-red study of ethylene chlorohydrin, that such a ring was present, even in the vapour state. This has been confirmed by Bastiansen (*Acta Chem. Scand.*, 1949, **3**, 415) who used the electron-diffraction technique. The existence of a stable ring structure is not compatible with the reorganized configuration required, during bimolecular reaction, by an intermediate transition complex. Such a transition complex would be (VI) for



ethylene dibromide, which reacts by a bimolecular mechanism in similar nucleophilic reactions. For " cyclic " ethylene chlorohydrin, however, the transition complex could only be formed by disruption of the ring. Our experiments seem to indicate that conditions less drastic than a sealed tube at 135° do not sufficiently bring this about. In this connection, it is of interest that ethylene chlorohydrin was much less reactive than ethanol in forming a semiacetal with *lævo*-menthyl benzoylformate (Glazer and Turner, *J.*, 1949, S 169), again possibly owing to the inactivation of the chlorohydrin by internal ring formation.

Experimental.

Toluene-*p*-sulphonanilide and toluene-*p*-sulphon-*m*-nitroanilide were prepared in quantitative yield by condensing the amine with one equivalent of toluene-*p*-sulphonyl chloride in pyridine.

N-Benzyltoluene-p-*sulphon*-m-*nitroanilide*.—(*a*) A solution of toluene-*p*-sulphon-*m*-nitroanilide (5·7 g., 1 mol.) in dry ethanol (50 c.c.) was added to ethanolic sodium ethoxide [from sodium (0·5 g., 1·1 atoms) and ethanol (50 c.c.)], and freshly distilled benzyl chloride (3·0 g., 1·2 mols.) added. The whole was boiled under reflux for 6 hours, ethanol (50 c.c.) distilled off, and the residue poured into 5% aqueous sodium hydroxide (300 c.c.). When the mixture was shaken, a colourless, granular precipitate of *N-benzyltoluene-p-sulphon*-m-*nitroanilide* separated, having m. p. 120—121° (Found: C, 62·8; H, 4·8; N, 7·55. $C_{20}H_{18}O_4N_2S$ requires C, 62·8; H, 4·75; N, 7·3%) (6·0 g., 80%). The m. p. was unaffected on crystallisation from alcohol. Acidification of the sodium hydroxide extract yielded 1·1 g. (19%) of unchanged toluene-*p*-sulphon-*m*-nitroanilide.

(*b*) Toluene-*p*-sulphonyl chloride (0·9 g., 1·1 mols.) was added to a solution of *N*-benzyl-*m*-nitroaniline (1·0 g., 1·0 mol.) in pyridine (2 c.c.). The mixture was warmed to 70°, cooled, and poured into excess of dilute hydrochloric acid. The resulting precipitate was washed with dilute acid and water. Crystallisation from ethanol gave colourless crystals, m. p. 120° (1·0 g., 60%).

NN′-p-*Xylylenebis*(*toluene*-p-*sulphon*-m-*nitroanilide*).—A solution of toluene-*p*-sulphon-*m*-nitroanilide (5·0 g., 1 mol.) in dry methanol (50 c.c.) was added to methanolic sodium methoxide [from sodium (0·4 g., 1·0 atom) and methanol (50 c.c.)]. A saturated solution of *p*-xylylene dibromide (4·5 g., 1 mol.) in ethanol was then added and the whole boiled under reflux for ½ hour, during which time a pale yellow flocculent precipitate was formed. The mixture was cooled and filtered. Crystallisation from benzene gave colourless crystals of NN′-p-*xylylenebis*(*toluene*-p-*sulphon*-m-*nitroanilide*), m. p. 193—194° (Found: C, 60·0; H, 4·7; N, 8·5. $C_{34}H_{30}O_8N_4S_2$ requires C, 59·5; H, 4·4; N, 8·2%) (8·0 g., 68%).

N-2-*Bromoethyltoluenesulphonanilide*.—A solution of toluene-*p*-sulphonanilide (5·0 g., 1 mol.) in dry ethanol (50 c.c.) was added to ethanolic sodium ethoxide [from sodium (0·5 g., 1·1 atoms) and ethanol (50 c.c.)]. Freshly distilled ethylene dibromide (3·8 g., 1 mol.) was added and the whole boiled under reflux for 3 hours. Some ethanol (50 c.c.) was distilled off and the remaining solution poured into 5% aqueous sodium hydroxide (300 c.c.). A colourless granular precipitate of N-2-*bromoethyltoluene*-p-*sulphonanilide*, m. p. 89—90° (1·1 g., 15%), was slowly deposited. Crystallisation from ethanol gave colourless crystals, m. p. 89—90° (Found: Br, 21·9. $C_{15}H_{16}O_2NBrS$ requires Br, 22·6%). Unchanged toluene-*p*-sulphonanilide (4·1 g., 82%) was recovered by acidifying the sodium hydroxide extract.

N-2-*Bromoethyltoluenesulphon*-m-*nitroanilide*, similarly prepared (reflux for 11 hours; yield 13%), crystallised from alcohol–acetone as colourless crystals, m. p. 117·5° (Found: Br, 19·4. $C_{15}H_{15}O_4N_2BrS$ requires Br, 20·0%).

N-2-*Methylallyltoluene*-p-*sulphonanilide*, prepared from the sodium salt of toluene-*p*-sulphonanilide and freshly distilled 2-methylallyl chloride in dry ethanol under reflux for 3 hours, was obtained as colourless crystals, m. p. 110—111° (from ethanol) (80%) (Found: C, 68·0; H, 6·6; N, 4·5. $C_{17}H_{19}O_2NS$ requires C, 67·7; H, 6·4; N, 4·7%). The corresponding m-*nitroanilide* (prep.: 7½ hours under reflux) was deposited from ethanol as colourless crystals, m. p. 109—109·5° (48%) (Found: N, 7·9. $C_{17}H_{18}O_4N_2S$ requires N, 8·1%).

Hydrogenations.—Reduction of the foregoing nitro-compound (5·7 g.) in acetic acid (90 c.c.) with platinum dioxide as catalyst gave N-iso*butyltoluene*-p-*sulphon*-m-*nitroanilide* as lemon-yellow crystals (from ethanol), m. p. 125° (4·5 g., 79%) (Found: C, 59·0; H, 6·0; N, 7·8. $C_{17}H_{20}O_4N_2S$ requires C, 58·6; H, 5·8; N, 8·0%). The reduction was stopped after 40 minutes to prevent reduction of the nitro-group.

Similar hydrogenation of *N*-2-methylallyltoluene-*p*-sulphonanilide gave *N-iso*butyltoluene-*p*-sulphonanilide (Hickinbottom, *J.*, 1930, 992), m. p. 122—123° (93%).

N-2-*Hydroxyethyltoluene*-p-*sulphon*-m-*nitroanilide*.—Toluene-*p*-sulphon-*m*-nitroanilide (4·75 g., 1 mol.), ethylene chlorohydrin (3·0 g., 2·3 mols.), potassium hydroxide (2·5 g.), and ethanol (10 c.c.) were heated (135°) in a sealed tube for 6 hours. The product was poured into excess of dilute alkali; gummy brown crystals separated and were purified by two precipitations with water from acetone–alcohol solution. N-2-*Hydroxyethyltoluene*-p-*sulphon*-m-*nitroanilide* separated as orange crystals, m. p. 65—66° (~100%) (Found: C, 53·0; H, 4·9; N, 8·1. $C_{15}H_{16}O_5N_2S$ requires C, 53·6; H, 4·8; N, 8·3%).

When the sodium salt of the sulphonanilide was heated under reflux with ethylene chlorohydrin (or iodohydrin) in anhydrous ethanol, alcoholic sodium hydroxide, or toluene (in the last case the presence of copper-bronze catalyst had no effect), or when the sulphonanilide was heated under reflux with ethylene chlorohydrin in pyridine, the original sulphonanilide was recovered quantitatively.

Analyses for C, H, and N are by Drs. Weiler and Strauss, Oxford.

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[*Received, September, 20th*, 1950.]

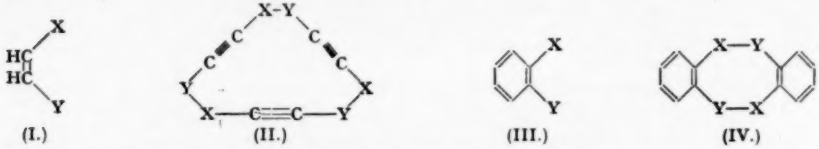
41. *Eight- and Higher-membered Ring Compounds. Part I. General Introduction.*

By Wilson Baker, J. F. W. McOmie, and W. D. Ollis.

A brief review is given of reactions leading to the formation of large-ring compounds in which ring closure is aided by the device of having the atoms concerned held in a number of rigid groups. Thus, for example, *ortho*-disubstituted benzenes may give rise to eight- (IV), twelve-, and higher-membered rings, *meta*-disubstituted benzenes to ten-membered rings (V), and *para*-disubstituted benzenes to eighteen-membered rings (VI).

The difficulties attending the preparation of many-membered ring compounds from open-chain structures are mainly due to the possibility of rotation about the bonds joining the atoms of which the chains are composed, so that the chance of atoms widely separated along the chain coming within reacting distance becomes rapidly smaller with increasing chain length. Two methods which have been widely used for overcoming this difficulty are the high-dilution technique due to Ziegler (Ziegler, Eberle, and Ohlinger, *Annalen*, 1933, **504**, 94), which minimises the possibility of intermolecular reaction but does not affect the intramolecular cyclisation, and recently the use of the acyloin reaction, where the reactive terminal groups of the chain are restricted in movement by adsorption on the surface of metallic sodium (Prelog, Frenkiel, Kobelt, and Barman, *Helv. Chim. Acta*, 1947, **30**, 1741; Stoll and Hulstkamp, *ibid.*, pp. 1815, 1822; Hansley, U.S.P. 2,226,268; Prelog, *J.*, 1950, 420).

A third method which does not yet appear to have been deliberately exploited for this purpose is to restrict the rotational possibilities by the device of having a number of atoms composing the chain held in the form of a rigid group or groups. The simplest possibility is the formation of an eight-membered cyclic compound by combination of molecules of the *cis*-olefin type, (I), but in practice the possibility of *cis–trans*-isomerisation might frequently raise



(I.) (II.) (III.) (IV.)

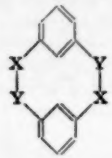
difficulties. In formulæ (I)—(VI), X and Y represent appropriate uni- or bi-valent radicals, and cases where X = Y are included. Another formally simple type in the aliphatic series is a triple combination of a suitably substituted acetylene X–C≡C–Y; this linear molecule might give rise to a twelve-membered ring compound (II), but such reactions have not yet been described and we have encountered difficulties in the preparation of suitably substituted acetylenes. The same principle is involved in the dimerisation of butadiene to *cyclo*octadiene (Ziegler and Wilms, *Annalen*, 1950, **567**, 1), and of 2-chlorobutadiene to a dichloro*cyclo*octadiene (Cope and Bailey, *J. Amer. Chem. Soc.*, 1948, **70**, 2305; Cope and Schmitz, *ibid.*, 1950, **72**, 3056), and may also be operative in the polymerisation of acetylene to *cyclo*octatetraene, if vinylacetylene is an intermediate (see Baker, *Endeavour*, 1950, **9**, 36).

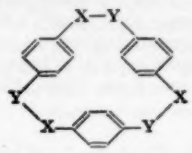
In practice a simpler approach is to secure the required rigidity by using, for example, an *ortho*-disubstituted benzene derivative (III). There are many examples in the literature of the formation of eight-membered ring compounds from such rigid four-membered units, and the formation of larger ring systems containing, for example, twelve-, sixteen-, and higher-membered rings from three, four, and larger numbers of such units is also possible. Recorded cases include the formation of the salicylides, cresotides, sulphonylides, anthranilides, etc., but the simplest are the production of *s*-dibenz*cyclo*octadiene (IV; X = Y = CH_2) and *s*-tribenz*cyclo*dodecatriene from *o*-xylylene dibromide by the action of sodium (Baker, Banks, Lyon, and Mann, *J.*, 1945, 27), and the reason why the first two authors undertook the work there described was to investigate the possibility of the formation of large-ring compounds, bearing in mind the considerations which have just been outlined (see footnote, Baker, Banks, Lyon, and Mann, *loc. cit.*).

Other interesting examples of the same kind are to be found in the work of Fieser and Pechet (*J. Amer. Chem. Soc.*, 1946, **68**, 2577) on the synthesis of *s*-dibenz*cyclo*octatetraene, of Rapson *et al.* on the synthesis of tetrabenz*cyclo*octatetraene from 2 : 2′-dibromodiphenyl (*J.*,

1943, 326), of Brown and Farthing (*Nature*, 1949, **164**, 915) who have isolated di-*p*-xylylene from the products of high-temperature pyrosynthesis of *p*-xylene, and of Ziegler and Luttringhaus (*Annalen*, 1934, **511**, 1) on the preparation of a 16-membered cyclic diketone, *m*-$C_6H_4<(CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_2{\cdot}CH_2)_2>C_6H_4$-*m*, from *m*-phenylenedipropionitrile.

(V.)





(VI.)

The foregoing ideas may be extended to the *meta*- and *para*-disubstituted aromatic compounds. Thus di-*m*-xylylene, a molecule of type (V) containing a ten-membered ring is readily prepared from *m*-xylylene dibromide and sodium (Baker, McOmie, and Norman, *Chem. and Ind.*, 1950, 77), and *p*-xylylene dibromide similarly yields tri-*p*-xylylene with an eighteen-membered ring, a molecule of novel, essentially triangular type (VI), derived from three linear units (cf. II) (Baker, McOmie, and Miss J. M. Norman, unpublished investigation). Very many variants of the foregoing types of reaction are clearly possible by altering the nature of the reacting groups X and Y, and the object of the work to be described in this series of papers is to investigate the formation, properties, and stereochemistry of large-ring compounds prepared from smaller, rigid assemblies of atoms. Of particular interest is the possibility that compounds of the type (IV) may be able to exist in two stereoisomeric modifications (see Part II, following paper).

The naturally occurring macrocyclic compounds fall into two main types, the simple, large-ring ketones, lactones, etc., and the many-membered cyclic compound which contain a number of rigid aromatic groupings, *e.g.*, certain bisbenzyl*iso*quinoline alkaloids (see Kondo and Tomita, *Arch. Pharm.*, 1936, **274**, 72, where photographs of models are given; Todd *et al.*, *J.*, 1948, 2170; 1949, 2767; 1950, 1606) and *dextro*tubocurarine chloride (King, *J.*, 1948, 265). The porphyrins are probably synthesised in Nature from preformed pyrrole units (Maitland, *Quart. Reviews*, 1950, **4**, 45), but here a central metal atom may also be involved. The synthesis of the sixteen-membered porphyrin ring has, however, been achieved in the laboratory from two almost rigid fragments (see, for example, Gilman, "Organic Chemistry," 2nd Edn., 1942, Vol. II, p. 1282) without, at least deliberate, participation of a polyvalent metal.

The phthalocyanines, although macrocyclic and composed of four rigid groups, are built up around a central metal atom in the form of four fused rings so that, although the rigid group principle is operating, it is not involved in quite the same way.

The following two papers in this series deal with the anhydro-derivatives of salicylic acid and three of the cresotic acids. These compounds contain eight-, twelve-, sixteen-, and twenty-four-membered rings.

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42. *Eight- and Higher-membered Ring Compounds. Part II. Di-, Tri-, Tetra-, and Hexa-salicylides.*

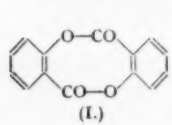
By WILSON BAKER, W. D. OLLIS, and T. S. ZEALLEY.

An account is given of previous work on the anhydrosalicylic acids, and of their complete re-investigation which has been carried out. The compounds formerly described as α- and β-disalicylides have proved to be *cis*-disalicylide (I), and trisalicylide (IV) respectively. Polysalicylide is shown to be hexasalicylide (VI). The hydrolysis of these compounds and their reaction with benzylamine have been studied, and their stereochemistry is discussed.

THE anhydro-derivatives of salicylic acid were chosen for early investigation in this work because, although they had been previously extensively examined there were some discrepancies in the literature, and because several such compounds had been described including two disalicylides and a tetrasalicylide (V). The two disalicylides (I) were originally supposed to be structurally different (R. Anschütz, *Ber.*, 1919, **52**, 1875; *J. pr. Chem.*, 1922,

105, 158; R. Anschütz and Riepenkröger, *Annalen*, 1924, **439**, 1), but Höhn later suggested (Richter–Anschütz, " Chemie der Kohlenstoff-Verbindungen," 1935, Vol. II, 2, 393) that they were geometrical isomers possessing " chair " and " trough " structures.

Stereoisomerism of this type has been discussed for the general case by Baker, Banks, Lyon, and Mann (*J.*, 1945, 27, where photographs of models are given), who showed that the centrosymmetrical *trans-* (or " chair ") form is rigid, whilst the *cis-* (or " trough ") form is mobile. The forms are interconvertible only by passage through a highly strained configuration or by breaking and reforming of a bond (cf. Roberts, *J. Amer. Chem. Soc.*, 1950, **72**, 3300). L. Anschütz and Neher (*J. pr. Chem.*, 1941, **159**, 264; *Ber.*, 1944, **77**, 634), in discussing the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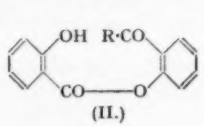
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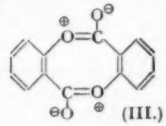
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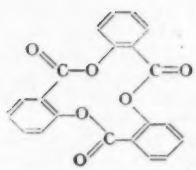
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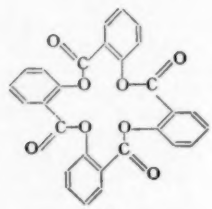
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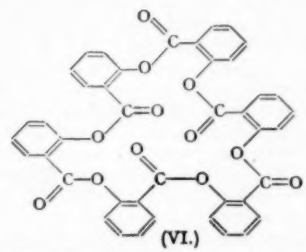

(VI.)

possible stereoisomerism of α- and β-" disalicylide " (see later) referred to the difficulty that, whereas the α-form is readily prepared from, and converted into, salicyloylsalicylic acid (" Diplosal ") (II; R = OH) and its derivatives, the β-form is not readily converted into this acid. L. Anschütz and Mayer (*J. pr. Chem.*, 1942, **159**, 343) and Meerwein (*Ber.*, 1941, **74**, 52) have commented on the absence of analogous cases of stereoisomerism, whilst Schönberg (*J.*, 1948, 891) has suggested that the two forms of disalicylide are stabilised by resonance which would give some double-bond character to the bridge carbon–oxygen bonds (see III). It appeared to the present authors that although resonance should favour the extreme *cis*-configuration, it should cause the *trans*-form, where resonance is scarcely possible in the ester groups, to be relatively less stable (*Nature*, 1949, **164**, 1049), and in view of these considerations it was felt desirable to re-investigate the anhydrosalicylic acids *de novo*. The chief result, already briefly reported (*loc. cit.*), has been to show that " β-disalicylide " is in fact trisalicylide (IV), containing a twelve-membered ring, and it has now been established that " polysalicylide " is hexasalicylide (VI) containing a twenty-four-membered ring.

The table gives the four known salicylides, previous authors (full references are given elsewhere in the text), former names, melting points, and molecular weights.

cis-*Disalicylide and Trisalicylide.*

Treatment of salicylic acid either with carbonyl chloride in pyridine (Einhorn and Pfeiffer, *Ber.*, 1901, **34**, 2952) or with phosphorus oxychloride in pyridine (Einhorn and Mettler, *Ber.*, 1902, **35**, 3646) gave a compound, m. p. 200—201°, in the latter case in 5% yield, whose molecular weight (see Table) supported a disalicylide structure. We also find that the first reaction gives a very low yield of this compound. In 1919 R. Anschütz (*loc. cit.*) followed up the earlier work of W. H. Perkin, sen., who had prepared xanthone by the distillation of salicylic acid and acetic anhydride (*Ber.*, 1883, **16**, 339; *J.*, 1883, **43**, 35), by carrying out the same distillation under diminished pressure. He isolated an " α-disalicylide," m. p. 213°, and a " β-disalicylide," considered to be identical with the substance, m. p. 200—201°, already described by Einhorn *et al.*

We find that when *O*-acetylsalicylic acid is heated under diminished pressure, acetic acid first distils in slightly less than the calculated amount, leaving a residue which is probably a polymeric anhydride, $H[O{\cdot}C_6H_4{\cdot}CO]_n{\cdot}OH$. No crystalline products can be isolated from this material, but after distillation at 300—350° two salicylides can be isolated by crystallisation,

and it appears that thermal degradation of the polymer occurs on distillation. One salicylide, m. p. 234° (24—30% yield), corresponds except for the higher melting point with "α-disalicylide," and the other, m. p. 200° (9—24% yield), was shown by direct comparison to be identical with the salicylide prepared by either of Einhorn's methods. R. Anschütz and Riepenkröger (*Annalen*, 1924, **439**, 3) have also prepared α-disalicylide, m. p. 210—212°, by reaction of salicyloyl chloride with diethylaniline, and repetition of this reaction has given us a product, m. p. 234°, identical with that prepared from *O*-acetylsalicylic acid, and in addition a smaller quantity of the salicylide, m. p. 200°. It is of interest that Schroeter (*Ber.*, 1919, **52**, 2224) obtained a disalicylide, m. p. 234°, believed to be identical with Anschütz's α-disalicylide, from salicyloylsalicyloyl chloride, $HO{\cdot}C_6H_4{\cdot}CO{\cdot}O{\cdot}C_6H_4{\cdot}COCl$, by reaction with diethylaniline.

Author(s)	Name	M. p.	Mol. wt. average
	cis-*Disalicylide* (*M* 240).		
R. Anschütz (1919)	α-Disalicylide	213°	231*a*
Schroeter (1919)	Salosalicylide	234	227*a*, 250*b*, 250*h*
R. Anschütz and Riepenkröger (1924)	α-Disalicylide	210—212	—
L. Anschütz and Neher (1941)	,,	213	—
L. Anschütz and Neher (1944)	,,	213—218	—
This paper	*cis*-Disalicylide	234 (decomp.)	236*c*, 248*d*, 291*e*
	Trisalicylide (*M* 360).		
Einhorn and Pfeiffer (1901)	Disalicylide	200—201°	275*a*, 279*c*
Einhorn and Mettler (1902)	,,	200—201	—
R. Anschütz (1919)	β-Disalicylide	199—200	—
L. Anschütz and Neher (1941)	,,	199—200	—
L. Anschütz and Mayer (1942)	,,	—	260*a*, 238*d*, 264*f*, 258*g*
L. Anschütz and Neher (1944)	,,	197—203	—
This paper	Trisalicylide	200	338*c*, 378*d*, 395*e*, 362*f*, 365*g*, 354 ± 10*i*
	Tetrasalicylide (*M* 480).		
R. Anschütz (1892; 1893)	Salicylide	261—262° 260—261	—
R. Anschütz and Schroeter (1893)	Tetrasalicylide	—	472*a*
Schroeter and Eisleb (1909)	,,	—	455*a*, 483*b*, 252*h*, 240 (443)*d*
Schroeter (1919)	Chloroform salicylide	—	—
Jusa and Janovitch (1938)	Tetrasalicylide	263	501*g*
This paper	,,	298—300	497*d*
	Hexasalicylide (*M* 720).		
R. Anschütz and Schroeter (1893)	Polysalicylide	322—325°	—
This paper	Hexasalicylide	375 (decomp.)	710 ± 20*i*

a = phenol (cryoscopic); *b* = nitrobenzene (cryoscopic); *c* = benzene (ebullioscopic); *d* = chloroform (ebullioscopic); *e* = dioxan (ebullioscopic); *f* = dioxan (cryoscopic); *g* = camphor (Rast); *h* = nitrobenzene (ebullioscopic); *i* = *X*-ray crystallographical method.

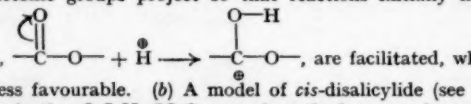
Re-determination of the molecular weights of these two salicylides by a variety of methods (see Table and Experimental section; also *Nature*, 1949, **164**, 1049) proved that the compound, m. p. 234°, is a disalicylide (I), but that the substance, m. p. 200°, is, without any possibility of doubt, trisalicylide (IV). The latter result is not in agreement with the molecular weights previously recorded (see Table), and the reason for these discrepancies is not clear. We have found, however, that consistent results are not obtained unless the solvents (particularly chloroform) are very carefully purified.

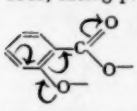
The disalicylide has been characterised as *cis*-disalicylide by determination of its dipole moment, which is 6·26 D. (Edgerley and Sutton, *Nature*, 1949, **164**, 1050; and forthcoming paper, "The stereochemistry of the salicylides and some related compounds," *J.*, in the press), and we therefore propose that the names α- and β-disalicylide be discarded and replaced by *cis*-disalicylide and trisalicylide respectively. Through the kindness of Professor L. Ansüchtz and Dr. Neher, we have been able to exchange specimens of these salicylides, and the complete identity of their α- and β-disalicylides with our *cis*-disalicylide and trisalicylide respectively has been proved by mixed-melting-point determinations, *X*-ray powder photographs (for which we are indebted to Dr. H. F. Kay and Miss B. Tucker of this University), and molecular-weight determinations. Professor L. Anschütz has accepted our identification of β-disalicylide as trisalicylide and at his request (letter dated 5th April, 1950) we quote his new molecular weights for α- and β-salicylides determined (at very high dilution owing to lack

of material) ebullioscopically in chloroform: α-compound, 217, 265; β-compound, 325, 368. It may be remarked that the melting point of *cis*-disalicylide depends to an appreciable extent on the rate of heating, and that our (corrected) melting point of 234° is obtained by rapid heating. Recent Raman spectra (Kohlrausch and Kahovec, *Monatsh.*, 1943, **74**, 333) and ultra-violet spectroscopic investigations (Wasmer, *Ber.*, 1949, **82**, 342) were interpreted in terms of *cis*- and *trans*-disalicylide forms, and now require re-interpretation in terms of *cis*-disalicylide and trisalicylide structures. Infra-red studies of the salicylides are being carried out by Mr. L. N. Short of the Physical Chemistry Laboratory, Oxford (forthcoming publication).

All the salicylides react with excess of alkali to give salicylic acid and with excess of benzylamine to give *N*-benzylsalicylamide. With methylmagnesium iodide, *cis*-disalicylide yields a mixture containing the dimeride of *o*-hydroxy*iso*propenylbenzene.

cis-Disalicylide is chemically the most reactive of the salicylides and under mild conditions gives derivatives of salicyloylsalicylic acid (II). Thus, with one equivalent of sodium hydroxide it gives salicyloylsalicylic acid (II; R = OH), with methanolic hydrogen chloride it gives methyl salicyloylsalicylate (II; R = OMe), with aniline it gives *O*-salicyloylsalicylanilide (II; R = NHPh), and with one equivalent of benzylamine it gives *N*-benzyl-*O*-salicyloylsalicylamide (II; R = $CH_2Ph{\cdot}NH$). When heated with glacial acetic acid containing about 5% of water, *cis*-disalicylide gives mainly salicyloylsalicylic acid (II; R = OH); under similar conditions phenyl benzoate is unaffected. With these reagents trisalicylide reacts much more slowly and only simple derivatives of salicylic acid can be isolated; we have utilised the greater reactivity of *cis*-disalicylide towards acetic acid to remove *cis*-disalicylide from crude trisalicylide.

In connection with the higher degree of reactivity of *cis*-disalicylide compared with trisalicylide and, in the case of acid hydrolysis, phenyl benzoate, two factors may be mentioned. (*a*) In *cis*-disalicylide the lactonic groups project so that reactions initially involving the carbonyl oxygen atoms, *e.g.*,  , are facilitated, whereas in trisalicylide steric factors are less favourable. (*b*) A model of *cis*-disalicylide (see Fig. 1B, *J.*, 1945, facing p. 28) shows that in the $\cdot O{\cdot}C_6H_4{\cdot}CO{\cdot}O\cdot$ groupings the benzene rings and the ester groups are inclined at an angle of almost 90° to one another, so that there can be little resonance interaction between them of the type represented by the formula inset. In trisalicylide, however, these groups are almost coplanar. This restricted resonance in *cis*-disalicylide would cause a relative decrease in its stability compared with that of trisalicylide, and would render its carbonyl-carbon atoms relatively more cationoid and more readily attacked by anionoid reagents such as aniline, benzylamine, or alkali.



It may finally be noted that di-*o*-xylylene (*s*-dibenzo*cyclo*octadiene) (formula IV of Part I; X = Y = CH_2) possesses the *trans*-configuration (Davidson, *J.*, 1945, 30) in contrast to disalicylide which possesses the *cis*-configuration. Resonance requirements (see above) undoubtedly govern the formation of the *cis*-disalicylide. We have been unable, in the present work, to find *trans*-disalicylide and it has recently been shown that, like the salicylides, the two forms of each of the three " dicresotides " are, in fact, *cis*-dicresotides and tricresotides (Baker, Gilbert, Ollis, and Zealley, *Chem. and Ind.*, 1950, 333; following paper). The only apparent case of a substance of the general type (IV; Part I) existing in *cis*- and *trans*-stereoisomeric forms is provided by the two dithymotides derived from 2-hydroxy-6-methyl-3-*iso*propylbenzoic acid (*o*-thymotic acid) (Spallino and Provenzal, *Gazzetta*, 1909, **39**, II, 330), and a re-investigation of these compounds is in progress. *

Tetrasalicylide and Hexasalicylide.

R. Anschütz (*Ber.*, 1892, **25**, 3506, 3512; *Annalen*, 1893, **273**, 73; D.R.-P. 68,960, 69,708, 70,614; " Friedländer," 1893, **3**, 822, 824, 825) and R. Anschütz and Schroeter (*Annalen*, 1893, **273**, 97) have reviewed the early work on anhydrosalicylic acids (Gerhardt, *Annalen*, 1853, **87**, 159; Kraut, *ibid.*, 1869, **150**, 13; Schiff, *ibid.*, 1872, **163**, 218) which they regarded as inconclusive, and themselves prepared two compounds by dehydration of salicylic acid with phosphorus oxychloride in toluene or xylene. These compounds were described as tetrasalicylide (V), m. p. 260—261°, and " polysalicylide," $[O{\cdot}C_6H_4{\cdot}CO]_n$, m. p. 322—325°, both of which could be hydrolysed to salicylic acid and gave phenyl salicylate with phenol. The tetrasalicylide was

* *Added in Proof.*—It has now been found by Mr. B. Gilbert in this laboratory that these two supposed dithymotides are, in fact, di- and tri-thymotides.

characterised as a well-crystalline adduct with two molecules of chloroform (see *Ber.*, 1892, **25**, 3512). The molecular-weight determinations carried out in phenol could not be regarded as satisfactory, and Schroeter and Eisleb (*Annalen*, 1909, **367**, 164) made further determinations with very varying results (see Table). Tetrasalicylide was later prepared by Jusa and Janovitch (*Monatsh.*, 1938, **71**, 202) and a determination of the molecular weight was made in camphor (Rast), but in view of our observations that Rast determinations are unsatisfactory with the salicylides we have re-investigated this compound.

By interaction of salicylic acid and phosphorus oxychloride in toluene we obtained a mixture of products from which were isolated trisalicylide (1%), tetrasalicylide (m. p. 298—300°; 35%) and hexasalicylide [m. p. 375° (decomp.); 35%]. Determination of the molecular weight of tetrasalicylide ebullioscopically in chloroform (Table) confirmed its structure, and in spite of its melting point being higher than previously recorded, the formation of the chloroform complex showed that it was identical with the substance already described. The salicylide, m. p. 375°, is apparently identical with R. Anschütz and Schroeter's " polysalicylide " in spite of its much higher melting point; it crystallises well from boiling nitrobenzene, but has too low a solubility in organic solvents for the molecular weight to be determined in the usual way. *X*-Ray crystallographical studies kindly undertaken by Dr. Kay and Miss Tucker have proved that it is a hexasalicylide (VI) and they have reported as follows:

" The specimens consisted of small, colourless, monoclinic crystals with external faces (001) ($1\bar{1}0$) (110). *X*-Ray and direct measurement give $\beta = 75° \pm 2°$. The unit-cell dimensions were determined by single-crystal methods as $a = 15{\cdot}0 \pm 0{\cdot}1$, $b = 14{\cdot}3 \pm 0{\cdot}1$, $c = 8{\cdot}1 \pm 0{\cdot}1$ A.; calculated volume of unit cell = $(1684 \pm 40) \times 10^{-24}$ c.c.

" The density was determined by the flotation method in three different solvent mixtures, giving the mean value $1{\cdot}407 \pm 0{\cdot}005$ g./c.c. Hence the number of $O{\cdot}C_6H_4{\cdot}CO$ groups per unit cell is 12. This permits either 2, 4, or 6 molecules per unit cell, and as it is not di- or tri-salicylide, it must be hexasalicylide.

" From these measurements the molecular weight observed is 710 ± 20."

Mr. I. S. Loupekine of the Department of Geology has measured the three principal refractive indices of hexasalicylide; he reports as follows:

" The optic axial plane is (010); $Z \wedge c$ (in acute β) $= 15° \pm 3°$ (+) $2V = 30°$ approx. Refractive indices ($\pm 0{\cdot}003$) are $\alpha = 1{\cdot}602$, $\beta = 1{\cdot}611$, $\gamma = 1{\cdot}760$. These optical data do not give any conclusive evidence of a planar structure."

The formation of tetra- and hexa- rather than di- and tri-salicylides under the above reaction conditions has led us to investigate the action of phosphorus oxychloride on the various salicylides themselves. Under the normal conditions of reaction, *cis*-disalicylide was converted into a mixture of tetra- and hexa-salicylides, no trisalicylide being detected; trisalicylide was partly unchanged and partly converted into tetrasalicylide and hexasalicylide; tetrasalicylide was partly unchanged and partly converted into hexasalicylide and a small amount of trisalicylide; hexasalicylide was unchanged. These results show that, in the presence of phosphorus oxychloride, the order of stability of the salicylides is *cis*-di- $\ll$ tri- $<$ tetra- $<$ hexa-salicylide; this may be partly due to the fact that the more insoluble products of higher molecular weight separate from the mixture during the reaction. The stabilities of the four salicylides towards hydrolysis with 2N-aqueous sodium hydroxide are also in the same order, but here again solubility may be a factor of importance (see Experimental). It may be recalled that L. Anschütz and Neher (*Ber.*, 1944, **77**, 638) found that treatment of salicyloylsalicylic acid with phosphorus oxychloride in xylene gave tri- (17·2%), tetra- (15·1%), and hexa-salicylide (53·8%).

Constellations of the Salicylides.

That disalicylide exists in the *cis*- rather than the *trans*-configuration appears to be caused by resonance requirements in the ester bridges; in the extreme folded form of the molecule there can be maximum contributions from the polarised ester groupings $-\overset{\ominus}{C}(=O)-\overset{\oplus}{O}-$. Two enantiomorphs of *cis*-disalicylide are possible (see Beilstein, " Handbuch der Organischen Chemie," 4th Edn., 1934, **19**, 172, 500), but an attempt to effect its resolution (L. Anschütz and Neher, *Ber.*, 1944, **77**, 637) was unsuccessful. In a model these antipodes are interconvertible by manipulation without distortion of the normal bond angles or bond lengths, but in the intermediate twisted phase (see illustration of the model of the structurally similar molecule of *s*-dibenz*cyclo*octadiene, Fig. 1A in *J.*, 1945, facing p. 28) there can be little or no resonance in the ester groups, and the oxygen atoms of the two carbonyl groups are

brought close together so that steric interaction might occur. There is thus a considerable energy barrier to be surmounted before the optically active forms can be interconverted, and it seems likely that resolution into stable enantiomorphs may be possible.

In approaching the question of the constellation of the salicylides the following requirements must be borne in mind: (*a*) resonance will be at a maximum within the ester groups, —O—CO—, and between these groups and the benzene rings only when the whole molecule is flat; (*b*) steric interaction of atoms or groups must be absent or only slight; (*c*) normal bond lengths and intervalency angles must be maintained as far as possible; (*d*) the *trans*-ester configuration is likely to be favoured rather than the *cis*- (Marsden and Sutton, *J.*, 1936, 1383).

These points have been considered in discussing the structures of disalicylide and trisalicylide (this and the forthcoming paper by Edgerley and Sutton). The latter most probably possesses three *trans*-ester groups (IV), and, to meet the requirements (*b*) and (*c*) above and to give a dipole moment in agreement with that found (2·95 D.), it is necessary to assume that the three ·C_6H_4·CO·O· groups are arranged on the faces of a low triangular-based pyramid.

With regard to tetrasalicylide (V), a structure in which the four planar O·C_6H_4·CO· units are arranged alternately up and down round the central square of four oxygen atoms, satisfies the requirements (*b*) and (*c*) and is compatible with its dipole moment of 2·07 D.

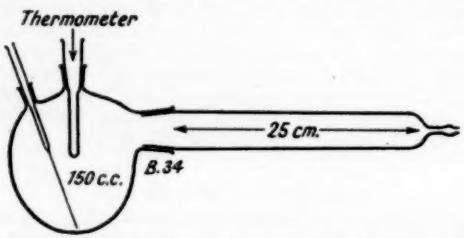
Pentasalicylide has not been found, and it seems most unlikely that it is formed in any of the reactions which have been investigated. It could not possess an alternating arrangement of the salicylide units, and its non-formation suggests that both tetra- and hexa-salicylide have some such arrangement of these groups. Hexasalicylide has a very low solubility in all solvents, and it has not been possible to determine its dipole moment. If we accept some alternating feature in its constellation, and as six *cis*-ester linkages are ruled out [see (*b*) and (*c*) above], it most probably has either six *trans*- or alternate *cis*- and *trans*-ester linkages. The latter is shown in formula (VI).

The complete solutions of these problems of constellation are only likely to be reached as the result of *X*-ray crystallographical studies.

Experimental.

All m. p.s are corrected. In cases where any decomposition occurred and the m. p. varied with the rate of heating, the m. p.s given were obtained by rapid heating, *i.e.*, the m. p. tube was placed in the bath, the temperature of which was steadily rising, some 5° below the final m. p. This procedure ensures the minimum accumulation of decomposition products before liquefaction, and gives a reproducible value. The discrepancies between some of our m. p.s and those previously recorded are almost certainly due to the difference between our method of m. p. determination with rapid heating and the more normal method of slower heating.

Action of Heat on O-Acetylsalicylic Acid (*cis-Disalicylide and Trisalicylide*).—(See R. Anschütz, *Ber.*, 1919, **52**, 1883.) The yields in this reaction are markedly dependent on the conditions of the experiment. The apparatus illustrated below was found to be the most satisfactory, the entire bulb being heated in an air-bath.



O-Acetylsalicylic acid (50 g.) was heated just above its m. p. (*ca.* 160°) at 15 mm. pressure and the temperature was increased slowly to *ca.* 200° during 0·5 hour, whereafter no more acetic acid (yield *ca.* 15 g.) was formed. The temperature was then increased to 300—350°/15 mm. and after 2—3 hours a semi-crystalline sublimate was obtained. This was triturated with 2N-sodium hydroxide, then with water, and dried (yield, 20—25 g.). Fractional crystallisation from chloroform gave *cis*-disalicylide (8—10 g., 24—30%) as colourless, twinned rhombs, m. p. 234° (decomp.) (Found: C, 69·8; H, 3·4. Calc. for $C_{14}H_8O_4$: C, 70·0; H, 3·4%). *cis*-Disalicylide crystallised unchanged from nitrobenzene or benzene (cf. Schroeter, *Ber.*, 1919, **52**, 2227).

The residue obtained from the chloroform mother-liquors was boiled with glacial acetic acid and a little water (5%) for 0·5 hour to hydrolyse remaining *cis*-disalicylide, and after removal of the acetic acid under reduced pressure, the residue was washed with 2N-sodium hydroxide, then water, dried, and

recrystallised several times from benzene, giving *trisalicylide* (3—8 g., 9—24%) as colourless needles, m. p. 200° (Found: C, 69·8; H, 3·2. $C_{21}H_{12}O_6$ requires C, 70·0; H, 3·4%).

In one experiment in which the temperature was maintained at 240—250°/0·5 mm., the sublimation required 6—7 hours for completion. The product (14 g.) from acetylsalicylic acid (50 g.), when worked up as before, gave *cis*-disalicylide (1·2 g.) and trisalicylide (0·4 g.), but the main product was xanthone (3·2 g.), m. p. 175°.

Action of Diethylaniline on Salicyloyl Chloride (cis-*Disalicylide and Trisalicylide*).—Salicyloyl chloride, prepared from salicylic acid (50 g.) (Kirpal, *Ber.*, 1930, **63**, 3190), was treated with diethylaniline as described by R. Anschütz and Riepenkröger (*Annalen*, 1924, **439**, 3). Repeated crystallisation of the final product from chloroform gave pure *cis*-disalicylide (10 g., 23%), m. p. and mixed m. p. 234° (decomp.).

Concentration of the original benzene–diethylaniline mother-liquors left a crystalline residue which, after several recrystallisations from benzene, was found to be trisalicylide (0·6 g., 1·4%), m. p. and mixed m. p. 200°.

Action of Phosphorus Oxychloride on Salicylic Acid (*Trisalicylide, Tetrasalicylide, and Hexasalicylide*).—Reaction of salicylic acid (50 g.) with redistilled phosphorus oxychloride (50 g.) in dry toluene (100 c.c.) at 100° was carried out as described by R. Anschütz and Schroeter (*Ber.*, 1892, **25**, 3506; *Annalen*, 1893, **273**, 76). The solid was collected and extracted with hot chloroform (500 c.c.), and the extract concentrated. The tetrasalicylide–chloroform complex separated as large, colourless rhombs which were heated at 100°/1 mm., giving tetrasalicylide (15 g., 35%) as opaque pseudomorphs, m. p. 298—300° (rapid heating) (Found: C, 69·6; H, 3·3. Calc. for $C_{28}H_{16}O_8$: C, 70·0; H, 3·4%). Recrystallisation from benzene gave colourless plates, m. p. 298—300°. The loss in weight when a freshly prepared specimen of the tetrasalicylide–chloroform *complex* (4·358 g.) was heated at 100°/1 mm. was 33·5%; $C_{28}H_{16}O_8.2CHCl_3$ requires $CHCl_3$, 33·2%.

The chloroform-insoluble material (15·3 g., 35%) was recrystallised form boiling nitrobenzene (1·5 l.), giving *hexasalicylide* as colourless, microcrystalline needles, m. p. 375° (rapid heating, decomp.; this m. p. was markedly dependent on the rate of heating) (Found: C, 69·8; H, 3·4. $C_{42}H_{24}O_{12}$ requires C, 70·0; H, 3·4%). Hexasalicylide very slowly sublimes unchanged at 200—250°/0·1 mm.

The original toluene solution obtained by filtration of the reaction mixture was washed with 2N-sodium hydroxide (acidification gave salicylic acid, 2·6 g., 5%), and a small amount of a sparingly soluble sodium salt separated at the interface. The toluene layer yielded a residue which, when recrystallised from benzene, gave trisalicylide (0·3 g., 1%), m. p. and mixed m. p. 200°.

Alkaline Hydrolysis of the Salicylides.—The finely powdered salicylides were heated at 100° with excess of 2N-sodium hydroxide till dissolution was complete; acidification then gave salicylic acid, m. p. and mixed m. p. 156° in each case. The times required for complete dissolution were: *cis*-disalicylide, 20 minutes; trisalicylide, 2 hours; tetrasalicylide, 12 hours; hexasalicylide, 48 hours. The yields of salicylic acid were 93, 87, 85, and 86% respectively.

Similarly, phenyl benzoate required 50 minutes at 100° for complete dissolution and gave benzoic acid (83%).

Reaction of the Four Salicylides with Excess of Benzylamine.—The salicylides were each refluxed for 3 hours with excess of benzylamine and a trace of ammonium chloride, and the cooled products poured into dilute hydrochloric acid. The solids were collected and dissolved in 2N-sodium hydroxide, and the solutions filtered and acidified with dilute hydrochloric acid. The precipitates were recrystallised from aqueous ethanol, giving in each case *N*-benzylsalicylamide, m. p. and mixed m. p. with an authentic specimen 136° (Dermer and King, *J. Org. Chem.*, 1943, **8**, 168, give m. p. 136·5—137°). The yields were: *cis*-di- 95, tri- 89, tetra- 85, and hexa-salicylide 85%.

N-Benzyl-O-salicyloylsalicylamide.—*cis*-Disalicylide (1 g.) was refluxed with benzylamine (0·45 c.c.) in benzene (80 c.c.) for 7 hours. Removal of the solvent gave a solid (m. p. 106°) which, after crystallisation from aqueous ethanol and then from benzene–light petroleum (b. p. 60—80°), gave *N-benzyl-O-salicyloylsalicylamide* (0·9 g., 62%) as colourless needles, m. p. 112° (Found: C, 72·8; H, 5·0; N, 4·8. $C_{21}H_{17}O_4N$ requires C, 72·6; H, 5·0; N, 4·0%).

Formation of Salicyloylsalicylic Acid ("*Diplosal*") *from* cis-*Disalicylide.*—(a) *Alkaline hydrolysis.* *cis*-Disalicylide (1 g.) in dioxan (50 c.c.) and sodium hydroxide (0·16 g.) in water (20 c.c.) were heated at 100° for 15 minutes and then concentrated under reduced pressure, water was added, and the mixture filtered and acidified. The precipitate (0·47 g., m. p. 110—120°) was collected, washed, and dried, and salicylic acid removed by 3 hours' heating at 100°/1 mm. The residue (0·2 g.) was recrystallised from benzene (1 c.c.), giving salicyloylsalicylic acid, m. p. 148—149° (cf. L. Anschütz and Neher, *loc. cit.*, who give m. p. 148°).

(b) *Acid hydrolysis.* *cis*-Disalicylide (1 g.) and 95% acetic acid (50 c.c.) were boiled under reflux for 0·5 hour, the solvents were removed under reduced pressure, and the residue was triturated with cold 2N-sodium hydroxide. The insoluble material (200 mg.) was collected and identified as unchanged *cis*-disalicylide, m. p. and mixed m. p. 232—234°. Acidification of the filtrate gave a precipitate (670 mg.; m. p. 138—141°) which gave salicylic acid (120 mg., 11%; m. p. 156°) on sublimation at 100°/0·5 mm. for 3 hours, and the residue (550 mg., 51%) was salicyloylsalicylic acid, m. p. and mixed m. p. 148—149°.

In similar experiments with phenyl benzoate, the recovery of starting material was 94% after boiling under reflux for 0·5 hour and 87% after 3 hours; no benzoic acid was detected.

Reaction of cis-*Disalicylide with Methylmagnesium Iodide.*—To a solution of methylmagnesium iodide, prepared from magnesium (7·2 g.) and methyl iodide (4·2 g.) in ether (100 c.c.), was added a

suspension of *cis*-disalicylide (3 g.) in benzene (100 c.c.). After boiling under reflux for 4 hours the mixture was poured on ice, acidified with dilute hydrochloric acid, and extracted with ether. The extract was washed with 2N-sodium hydroxide and water and dried ($MgSO_4$), and the ether removed. The residue was distilled, giving a yellow resinous material (1·2 g.; b. p. 140—150°/0·4 mm.) which separated from light petroleum (b. p. 40—60°) as colourless tablets, m. p. 95°; this compound gave an acetyl derivative, m. p. 95°. Mixed m. p.s of these substances with the dimeride of *o-iso*propenylphenol and its acetyl derivative (Fries, Gross-Selbeck, and Wicke, *Annalen*, 1914, **402**, 306) showed no depression. This dimeride is probably 2′-hydroxy-2 : 4 : 4-trimethylflavan (Baker and Besly, *J.*, 1940, 1103).

Phenyl benzoate and methylmagnesium iodide gave phenol (95%) and dimethylphenylcarbinol (98%) under the same conditions.

Reaction of Tetrasalicylide with Acetic Anhydride and Concentrated Sulphuric Acid.—This reaction is claimed by Schroeter (*Ber.*, 1919, **52**, 2230) to yield "acetyl-tetrasalicylic acid," $CH_3{\cdot}CO{\cdot}(O{\cdot}C_6H_4{\cdot}CO)_4{\cdot}OH$, as an amorphous material, m. p. *ca.* 120°, but we have been unable to confirm this and have isolated only salicyloylsalicylic acid. A mixture of acetic anhydride (10 c.c.), concentrated sulphuric acid (6·5 c.c.), and glacial acetic acid (0·12 c.c.) was added to a solution of tetrasalicylide (1 g.) in acetic anhydride (10 c.c.). After 5 minutes' heating at 100°, the mixture was cooled rapidly and poured on ice, and the solid (0·9 g.; m. p. 70—80°) collected, washed, dried, and then shaken with cold ether (70 c.c.). The insoluble residue (0·15 g.) was recrystallised from benzene, giving tetrasalicylide, m. p. and mixed m. p. 295—297°. The ethereal solution was extracted with dilute sodium hydroxide solution; acidification gave a solid (0·36 g., m. p. 128—130°) which was recrystallised from benzene–light petroleum (b. p. 60—80°), giving salicyloylsalicylic acid (diplosal) as fibrous needles, m. p. 131—132°. When the specimen was kept the m. p. rose to 148—149° and gave no depression with an authentic specimen (see above) (Found: C, 64·9; H, 4·0. Calc. for $C_{14}H_{10}O_5$: C, 65·1; H, 3·9%).

Action of Phosphorus Oxychloride on the Four Salicylides.—Each salicylide (2 g.), phosphorus oxychloride (2·4 g.), and toluene (5 c.c.) were heated at 100° for 6 hours, water (0·15 g.) added, and the heating continued for 15 hours. More water was then added and the mixture worked up as described above for the reaction of salicylic acid with phosphorus oxychloride. *cis*-Disalicylide gave tetrasalicylide (25%) and hexasalicylide (55%); trisalicylide gave tetrasalicylide (19·5%), hexasalicylide (55%), and recovered trisalicylide (7·5%); tetrasalicylide gave trisalicylide (2%), recovered tetrasalicylide (49%), and hexasalicylide (27%); hexasalicylide was recovered quantitatively.

Determination of the Molecular Weights of the Salicylides.—The solvents were purified as follows. Anala R benzene was dried over sodium wire and fractionally distilled. The chloroform was washed with concentrated sulphuric acid, then water, dried over calcium chloride, and fractionally distilled. The chloroform was used within a few hours of purification. The dioxan was purified as recommended by Vogel ("Practical Organic Chemistry," 1948, p. 175). All solutes were heated under reduced pressure in a drying "pistol" before use, and were analytically pure. After the determinations the solutes were recovered quantitatively and with unchanged m. p.s by removal of the solvent under diminished pressure.

The ebullioscopic determinations were carried out in the Menzies–Wright apparatus (*J. Amer. Chem. Soc.*, 1921, **43**, 2314). In this method the molecular weight is usually determined after the addition of each solute pellet using equation (1), and the means of these values then calculated:

$$M = 100K'w/VF(x - x_0) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where M = the molecular weight of solute, K' = the ebullioscopic constant for 100 c.c. of solvent, the volume being measured at its boiling point, w = the weight of solute, V = the volume of solvent available for solution at the boiling point, F = the differential thermometer-conversion factor at the b. p., x = the difference between liquid heights in the differential thermometer for the solution at its b. p., and x_0 = the difference between liquid heights in the differential thermometer for the pure solvent at its b. p.

In the original method the accuracy of the results is controlled by x_0. This is undesirable for the reason given below, and the following modification was used. In our determinations the solute was added in the form of four pellets, and the five readings of the differential thermometer were plotted against the weight of solute (the maximum concentration of solute was <2%). In drawing a straight line through these points, most attention was paid to the last four, which were usually collinear, as the first point frequently did not lie exactly on the same straight line.

From equation (1),

$$x = Sw + x_0, \text{ where } S = 100K'/VFM \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and the slope S of the line can be determined after plotting x against w, from which the molecular weight was calculated.

The ebullioscopic constants K' used in these Menzies–Wright determinations were: benzene 32·0, chloroform 27·7 (Menzies and Wright, *loc. cit.*), and dioxan 34·6 (calculated from data given by Herz and Lorentz, *Z. physikal. Chem.*, 1929, **140**, 414). For the cryoscopic determination of molecular weight in dioxan we have used $K = 50{\cdot}1$ (previous reference).

Rast determination of the molecular weight of *cis*-disalicylide gave values of 312, 600, 707, and 272, which are clearly unreliable; the varying results are probably explained by the low solubility and instability of *cis*-disalicylide in molten camphor.

Microanalyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol. Determinations of molecular weights by Rast's method are by Drs. Weiler and Strauss.

THE UNIVERSITY, BRISTOL. [*Received, September 28th*, 1950.

43. *Eight- and Higher-membered Ring Compounds. Part III. Di-, Tri-, and Tetra-cresotides.*

By Wilson Baker, B. Gilbert, W. D. Ollis, and T. S. Zealley.

The anhydro-derivatives of *o*-, *m*-, and *p*-cresotic acids have been re-investigated. The α- and β-" dicresotides " are shown to be the eight-membered *cis*-dicresotides and the twelve-membered tricresotides respectively. Both di- and tri-cresotides are formed by heating *O*-acetylcresotic acids. The preparation of the sixteen-membered, hitherto unknown, tetra-*m*-cresotide is described. The stereochemistry of these substances and its relationship to that of the salicylides is discussed.

Anhydro-derivatives of cresotic acids have been investigated by R. Anschütz (*Ber.*, 1892, **25**, 3509), Schöpff (*ibid.*, p. 3642), R. Anschütz (*Annalen*, 1893, **273**, 88, 94; D.R.-P. 70,158, " Friedländer," 1893, **3**, 825), R. Anschütz and Schroeter (*Annalen*, 1893, **273**, 97), Einhorn and Pfeiffer (*Ber.*, 1901, **34**, 2953), Einhorn and Mettler (*ibid.*, 1902, **35**, 3644), R. Anschütz (*Annalen*, 1924, **439**, 8), and by L. Anschütz and Gross (*Ber.*, 1944, **77**, 644). The last workers have described two dicresotides (α- and β-forms) derived from each of the *o*-, *m*-, and *p*-cresotic acids (2-hydroxy-3-methyl-, 2-hydroxy-4-methyl-, and 2-hydroxy-5-methylbenzoic acids). It was suggested that these pairs of cresotides were related to the α- and β-" disalicylides," but it has now been shown (see preceding paper) that the α- and β-disalicylides are, in fact, *cis*-disalicylide and trisalicylide respectively. We have, therefore, undertaken a re-investigation of the cresotides derived from *o*-, *m*-, and *p*-cresotic acids, and a preliminary announcement of the results has been made (Baker, Gilbert, Ollis, and Zealley, *Chem. and Ind.*, 1950, 333).

L. Anschütz and Gross prepared their α-dicresotides by distillation of the *O*-acetylcresotic acids under diminished pressure. We find that this procedure gives at least two compounds in each case, namely the *cis*-dicresotide and tricresotide, with, in the case of *O*-acetyl-*m*-cresotic acid, a small amount of tetra-*m*-cresotide. These results are analogous to those obtained by the distillation of *O*-acetylsalicylic acid (see Part II, where formulæ are given for the corresponding salicylides).

The fact that these products are di- and tri-cresotides was established by ebullioscopic determination of their molecular weights in chloroform and benzene (see the table); the slight difference between these results and those previously published by us are due to the fact that we now use the modified method described in Part II in calculating the molecular weights. The table also gives other relevant details (literature references are given in the text).

All the *cis*-dicresotides melt with some decomposition and the melting points depend upon the rate of heating. We have used the method of rapid heating described in Part II, and this undoubtedly accounts for some of the discrepancies between the melting points now recorded and those previously given by other workers. The variability of the melting points of the α-compounds was noticed by Anschütz and Gross (*loc. cit.*) and it is presumed that our *cis*-dicresotides are identical with the α-dicresotides described by them.

L. Anschütz and Gross prepared " β-di-cresotides " in low yield by dehydration of the cresotic acids with phosphorus oxychloride in pyridine. We have re-investigated this reaction with *o*- and *m*-cresotic acids and have isolated more than one crystalline compound in each case, but the main products were non-crystalline polymers, probably $H[O{\cdot}C_7H_6{\cdot}CO]_n{\cdot}OH$. From *o*-cresotic acid, *cis*-di-, tri-, and tetra-*o*-cresotide were obtained; *m*-cresotic acid gave small amounts of *cis*-di- and tri-*m*-cresotide.

Comparison of the melting points of our tri-*m*- and tri-*p*-cresotides suggests that they are identical with the " β-di-*m*-cresotide " and the " β-di-*p*-cresotide " described by L. Anschütz and Gross (*loc. cit.*). The melting point which they give for " β-di-*o*-cresotide " (231—231·5°) is much lower than the melting point of tri-*o*-cresotide (264—265°). The reason for this difference is not clear, since the melting points of these trimers do not depend upon the rate of heating and they do not decompose at the melting point. It may be significant that we have found that the only satisfactory method of isolating pure tri-*o*-cresotide is by first sorting the mixtures by hand.

The tetra- and -*p*-cresotides were prepared by R. Anschütz (*Ber.*, 1892, **25**, 3509; *Annalen*, 1893, **273**, 88) by dehydration of the cresotic acids with phosphorus oxychloride in toluene at 100°. R. Anschütz and Schroeter (*Annalen*, 1893, **273**, 97) determined their molecular weights cryoscopically in phenol, but since it is known that such substances will react with phenol we

Author(s)	Name	M. p.	*M*, average
	cis-*Di*-o-*cresotide* (*M*, 268).		
Schöpff (1892)	*o*-Cresotic acid anhydride	224—225°	260 *b*
R. Anschütz (1924)	α-Di-*o*-cresotide	224—225	—
L. Anschütz and Gross (1944)	α-*o*-Dicresotide	232—233 (235—236)	267 *d*
This paper	*cis*-Di-*o*-cresotide	240 (decomp.)	283 *b*, 278
	Tri-o-*cresotide* (*M*, 402).		
Einhorn and Pfeiffer (1901)	*o*-Dicresotide	231·5	—
Einhorn and Mettler (1902)	,,	231—231·5	298 *b*
L. Anschütz and Gross (1944)	β-Di-*o*-cresotide	231—231·5 (232·5)	273 *d*
This paper	Tri-*o*-cresotide	264—265	390 *b*, 390 *d*
	Tetra-o-*cresotide* (*M*, 536).		
R. Anschütz (1892; 1893)	*o*-Homosalicylide or β-Cresotide	293—295	—
R. Anschütz and Schroeter (1893)	*o*-Homosalicylide or tetra-*o*-homosalicylide	—	527 *a*
This paper	Tetra-*o*-cresotide	299—300	542 *b*, 548 *d*
	cis-*Di*-m-*cresotide* (*M*, 268).		
L. Anschütz and Gross (1944) *	α-*m*-Dicresotide	217—218 (221—222)	276 *d*
This paper	*cis*-Di-*m*-cresotide	255 (decomp.)	265 *b*, 271 *d*
	Tri-m-*cresotide* (*M*, 402).		
Einhorn and Pfeiffer (1901)	*m*-Dicresotide	207·5	—
Einhorn and Mettler (1902)	,,	207—207·5	262 *c*
L. Anschütz and Gross (1944)	β-*m*-Dicresotide	207—207·5 (209)	267 *d*
This paper	Tri-*m*-cresotide	207—207·5	405 *b*, 399 *d*
	Tetra-m-*cresotide* (*M*, 536).		
This paper	Tetra-*m*-cresotide	305 (decomp.)	542 *b*, 542 *d*
	Hexa(?)-m-*cresotide*.		
R. Anschütz (1892; 1893)	*m*-Homopolysalicylide or Poly-γ-cresotide	292—294	—
This paper	Hexa(?)-*m*-cresotide	Above 380 (decomp.)	—
	cis-*Di*-p-*cresotide* (*M*, 268).		
R. Anschütz (1924)	α-Di-*p*-cresotide	197—199	264 *d*
L. Anschütz and Gross (1944)	α-*p*-Dicresotide	223—224 (225—226)	259 *d*
This paper	*cis*-Di-*p*-cresotide	235—235·5 (decomp.)	274 *b*, 273 *d*
	Tri-p-*cresotide* (*M*, 402).		
Einhorn and Pfeiffer (1901)	*p*-Dicresotide	243·5	—
Einhorn and Mettler (1902)	,,	243	293 *c*
L. Anschütz and Gross (1944)	β-*p*-Dicresotide	243 (245)	265 *d*
This paper	Tri-*p*-cresotide	244·5—245	404 *b*, 393 *d*
	Tetra-p-*cresotide* (*M*, 536).		
R. Anschütz (1892; 1893)	*p*-Homosalicylide or α-cresotide	295—297	—
R. Anschütz and Schroeter (1893)	*p*-Homosalicylide or tetra-*p*-homosalicylide	—	537 *a*
This paper	Tetra-*p*-cresotide	347 (decomp.)	548 *d*

a = phenol (cryoscopic); *b* = benzene (ebullioscopic); *c* = nitrobenzene (cryoscopic); *d* = chloroform (ebullioscopic).

M. p.s given in parentheses are micro-m. p.s given by L. Anschütz and Gross, using the Kofler method.

* There is some doubt about the nature of the product, m. p. 208—209° (molecular weight undetermined), prepared by R. Anschütz (*Annalen*, 1924, **439**, 12) by distillation of *O*-acetyl-*m*-cresotic acid and described as α-di-*m*-cresotide. On account of its m. p., L. Anschütz and Gross (*loc. cit.*) have suggested that it may be identical with their β-*m*-dicresotide (now known to be tri-*m*-cresotide), but its chemical properties described by R. Anschütz lead us to believe that it was more probably *cis*-di-*m*-cresotide.

have determined their molecular weights ebullioscopically in chloroform and, if sufficiently soluble, in benzene. *o*-Cresotic acid and phosphorus oxychloride in hot toluene gave only tetra-*o*-cresotide. Similarly, *p*-cresotic acid gave only tetra-*p*-cresotide. *m*-Cresotic acid similarly treated gave a mixture from which a very high-melting *m*-cresotide (m. p. >380°) and the hitherto unknown tetra-*m*-cresotide were isolated. This tetra-*m*-cresotide was identical with the very small amount of the tetra-*m*-cresotide formed during the distillation of *O*-acetyl-*m*-cresotic acid. This reaction of *m*-cresotic acid with phosphorus oxychloride in toluene is to be compared with the corresponding reaction of salicylic acid with phosphorus oxychloride in which it is known that tetrasalicylide and the high-melting hexasalicylide are formed (see Part II). The physical properties of the high-melting *m*-cresotide are very similar to those of hexasalicylide and, since the formation of pentamers and heptamers is unlikely (see Part II), it is very probable that this compound is hexa-*m*-cresotide.

It is of interest that the reaction of phosphorus oxychloride with *o*- and *p*-cresotic acids gives only tetracresotides; hexacresotides are not formed in these cases.

It may be noted that several of these large-ring compounds crystallise with solvent of crystallisation. Tetrasalicylide crystallises with two molecules of chloroform (R. Anschütz, *Ber.*, 1892, **25**, 3512; *Annalen*, 1893, **273**, 94; see also preceding paper), as does also tetra-*o*-cresotide (*idem*, D.R.-P. 70,158, *Friedl.*, 1893, **3**, 825); tetra-*m*-cresotide crystallises with one molecule of benzene; tri-*p*-cresotide also separates with benzene of crystallisation.

The Constellation of the Cresotides.—Dipole-moment determination (Edgerley and Sutton, forthcoming publication, "The stereochemistry of the salicylides and some related compounds," *J.*, in the press) show that the dicresotides all have the *cis*-configuration, as has *cis*-disalicylide. Like *cis*-disalicylide, they are chemically reactive, undergoing hydrolysis with hot, slightly diluted acetic acid, and reaction with methanolic hydrogen chloride at 100° to give the methyl esters of the cresotoylcresotic acids.

The three tricresotides probably possess structures very similar to the structure of trisalicylide, but that of tri-*o*-cresotide may be slightly modified to reduce steric interaction involving the methyl groups. The three tetracresotides and hexa-*m*-cresotide presumably have structures analogous to those of the corresponding salicylides.

Experimental.

M. p.s are uncorrected.

Action of Heat on O-*Acetyl-o-cresotic acid* (cis-*Di- and Tri-o-cresotide*).—*O*-Acetyl-*o*-cresotic acid (50 g.) was heated in the apparatus previously described (Part II). At *ca.* 170°/17 mm. acetic acid (*ca.* 10 g.) first distilled, followed at *ca.* 200° by a sublimate consisting mainly of *o*-cresotic acid. The temperature was gradually raised to 300°, and during 2 hours a sublimate was obtained, leaving finally a pitch-like residue. The sublimate (16 g.) was crystallised from chloroform (*ca.* 200 c.c.), giving *cis*-di-*o*-cresotide (3·8 g.), colourless needles, m. p. 240° (decomp.) (Found: C, 71·6; H, 4·4. Calc. for $C_{14}H_{12}O_4$: C, 71·6; H, 4·5%).

Concentration of the chloroform mother-liquors gave successive crops, each consisting of a mixture of needles and rhombs which were separated by hand. The needles on recrystallisation gave more *cis*-di-*o*-cresotide, m. p. and mixed m. p. 240°. The rhombic crystals after recrystallisation from benzene gave *tri-o-cresotide* (2·3 g.), m. p. 264—265° (Found: C, 71·9; H, 4·4. $C_{21}H_{18}O_6$ requires C, 71·6; H, 4·5%).

Reaction of o-*Cresotic Acid with Phosphorus Oxychloride in Pyridine.*—Satisfactory results were not obtained using the conditions given by L. Anschütz and Gross (*loc. cit.*), and a more concentrated solution in pyridine was used.

Redistilled phosphorus oxychloride (11·2 g.) was added dropwise to a stirred solution of *o*-cresotic acid (20 g.) in dry pyridine (100 c.c.). After being stirred for 7 hours and left overnight, the mixture was poured on ice, and the precipitate (16 g.) collected, washed, triturated with 2N-hydrochloric acid, then with 2N-sodium hydroxide, and water. The dried product (13·5 g.) was dissolved in a small quantity of hot chloroform, and the pure tetra-*o*-cresotide–dichloroform complex (0·7 g.; m. p. and mixed m. p. 299—300°) (see below) separated on cooling. The mother-liquors yielded *cis*-di-*o*-cresotide (0·6 g.), m. p. and mixed m. p. 240° (decomp.), and rhombic crystals of tri-*o*-cresotide, m. p. and mixed m. p. 264—265°, which were separated by hand and recrystallised from benzene.

Reaction of o-*Cresotic Acid with Phosphorus Oxychloride in Toluene* (*Tetra-o-cresotide*).—*o*-Cresotic acid (55 g.), redistilled phosphorus oxychloride (50 g.), and toluene (100 c.c.) were heated on a steam-bath for 11 hours, and then poured on ice (100 g.), and the solid (18·6 g.) was collected, washed, and dried. After trituration with 2N-sodium hydroxide and water, the solid (18·0 g.; m. p. 296—298°) was recrystallised from benzene, giving *tetra-o-cresotide* as colourless needles, m. p. 299—300° (Found: C, 71·4; H, 4·5. $C_{28}H_{24}O_8$ requires C, 71·6; H, 4·5%).

Tetra-o-cresotide, when crystallised from chloroform, gave the *dichloroform* complex as large, colourless rhombs (Found: loss on heating to constant weight at 100°/1 mm., 31·5. Calc. for $C_{28}H_{24}O_8,2CHCl_3$: loss, 30·8%).

Reaction of the Three o-*Cresotides with Benzylamine* (N-*Benzyl-o-cresotamide*).—*cis*-Di-*o*-cresotide (0·5 g.) was refluxed with benzylamine (1·5 c.c.) and a trace of ammonium chloride for 4 hours, and then poured into 2N-hydrochloric acid. The solid was collected and dissolved in 2N-sodium hydroxide, and the solution filtered and acidified. The precipitated *benzylamide* (0·8 g., 90%; m. p. 72—73°) separated from aqueous ethanol in colourless needles, m. p. 73° (Found: C, 74·7; H, 6·5; N, 5·6. $C_{15}H_{15}O_2N$ requires C, 74·6; H, 6·3; N, 5·8%).

Tri-*o*-cresotide and tetra-*o*-cresotide similarly gave the benzylamide, in 87 and 81% yields respectively.

Action of Heat on O-*Acetyl*-m-*cresotic Acid* (cis-*Di*-m-*cresotide*, *Tri*-m-*cresotide*, *and Tetra*-m-*cresotide*).—*O*-Acetyl-*m*-cresotic acid (50 g.; L. Anschütz and Gross, *loc. cit.*) was heated as previously described at 150°/18 mm., giving first acetic acid, and then at 250°/18 mm. a product (24·75 g.) which became semi-solid on cooling. It was collected, and washed first with cold and then hot light petroleum (b. p. 60—80°; 100 c.c. portions) [the washings gave a viscous oil (6·0 g.) from which no crystalline product could be isolated]. The insoluble material (17·4 g.) was washed with cold chloroform (40 c.c.); one of the components, which was present as large crystals, did not dissolve rapidly and was collected. This substance (5·2 g.), after four recrystallisations from benzene (40 c.c.), gave *cis*-di-*m*-cresotide (2·66 g.) as colourless prisms, m. p. 255° (decomp.). This m. p. was markedly dependent upon the rate of heating and reproducible results were only obtained by using a preheated oil-bath (Found: C, 71·9; H, 4·4. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%).

The chloroform filtrate was washed with 2N-sodium hydroxide (20 c.c.) and then with water, dried ($MgSO_4$), and distilled, leaving a solid (10·5 g.) which was triturated with hot benzene (50 c.c.). The insoluble material (4·0 g.) was crystallised from carbon tetrachloride (75 c.c.), and the resultant mixture was freed from *cis*-di-*m*-cresotide by three crystallisations from hot, slightly dilute acetic acid, giving a product (2·6 g.), m. p. 196—197°. Two further recrystallisations from acetic acid (150 c.c.) gave tri-*m*-cresotide (1·3 g.) as colourless needles, m. p. 207—207·5° (Found: C, 71·5; H, 4·4. Calc. for $C_{24}H_{16}O_6$: C, 71·6; H, 4·5%). The benzene filtrate gave a residue (3·7 g.) which was crystallised from ethanol (25 c.c.), then from acetic acid (5 c.c.), yielding colourless needles (0·18 g.), m. p. and mixed m. p. with tri-*m*-cresotide, 207°. Concentration of the acetic acid mother-liquors (to 2 c.c.) gave a fraction (0·20 g.), m. p. 210—284°, which, after recrystallisation 6 times from benzene (2 c.c.)–light petroleum (b. p. 60—80°; 1 c.c.) gave tetra-*m*-cresotide as the *benzene* complex (30 mg.) in colourless prisms, m. p. 305° (decomp.) (Found: C, 74·5; H, 4·5. $C_{32}H_{24}O_8,C_6H_6$ requires C, 74·4; H, 4·9%). This material was identical with that obtained by dehydration of *m*-cresotic acid with phosphorus oxychloride in toluene (see below).

Small amounts of 3:6-dimethylxanthone (m. p. 170—172°) were also isolated (L. Anschütz and Gross, *loc. cit.*, give m. p. 166°).

Reaction of m-*Cresotic Acid with Phosphorus Oxychloride in Pyridine.*—The method of L. Anschütz and Gross (*loc. cit.*) did not yield a solid product and the method was modified as follows. Re-distilled phosphorus oxychloride (2·8 g.) was added with stirring to *m*-cresotic acid (5 g.) in dry pyridine (25 c.c.). After 15 hours at room temperature, the mixture was poured on ice and water (250 g.) and centrifuged. The solid (2·2 g.; m. p. 124—200°) was collected, dissolved in chloroform (50 c.c.), washed with 5% sodium hydroxide (10 c.c.) and then water, and dried ($MgSO_4$), and the solvent removed, giving a solid (1·1 g.), m. p. 190—200°. Recrystallisation from benzene (20 c.c.) gave *cis*-di-*m*-cresotide (30 mg.), m. p. and mixed m. p. 250° (decomp.). The benzene mother-liquors yielded a product which was recrystallised from slightly diluted acetic acid and eventually gave tri-*m*-cresotide (30 mg.; m. p. and mixed m. p. 207—208°).

Reaction of m-*Cresotic Acid with Phosphorus Oxychloride* [*Tetra*-m-*cresotide and Hexa*(?)-m-*cresotide*].—*m*-Cresotic acid (50 g.), phosphorus oxychloride (50·5 g.), and dry toluene (100 c.c.) were heated on a steam-bath for 10 hours, and after 36 hours poured into ice-water (150 g.). The precipitate (15 g.) was collected, washed with 2N-sodium hydroxide and then water, dried, and recrystallised three times from boiling nitrobenzene (1·2 l.), from which it separated on cooling and very long standing. This *hexa*(?)-m-*cresotide* (4·3 g.) formed colourless, microcrystalline, rhombic plates which decomposed at 380° without melting (Found: C, 71·8; H, 4·5. $C_{48}H_{36}O_{12}$ requires C, 71·6; H, 4·5%).

The toluene layer (above) was washed with 2N-sodium hydroxide (2 × 25 c.c.) and then water, dried ($MgSO_4$), and distilled. The residue (5·1 g.) was recrystallised 6 times from benzene (30 c.c.)–light petroleum (b. p. 60—80°; 30 c.c.), giving tetra-*m*-cresotide as the *benzene* complex (1·3 g.) in colourless prisms, m. p. and mixed m. p. 305° (decomp.). The benzene was detected by the micro-modification of Ramsden's test for aromatic hydrocarbons (see Baker and Leeds, *J.*, 1948, 979) (Found: loss on heating to constant weight at 125°, 13·1. $C_{32}H_{24}O_8,C_6H_6$ requires loss, 12·7%). The resulting pseudomorphic *tetra*-m-*cresotide*, m. p. 305° (decomp.), was analysed (Found: C, 71·7; H, 4·2. $C_{32}H_{24}O_8$ requires C, 71·6; H, 4·5%).

p-*Cresotic Acid.*—The Kolbe–Schmitt synthesis of this acid described by Cameron, Jeskey, and Baine (*J. Org. Chem.*, 1950, **15**, 233) gives a maximum yield of 87% and requires high-pressure apparatus. The method given below gives a 48% yield and is carried out at atmospheric pressure.

p-Cresol (100 g.) was slowly added to sodium hydroxide (37 g.) in water (50 c.c.), and the paste was heated with stirring until dry enough to powder. The powder was heated and stirred at 170° for 4 hours in a stream of dry nitrogen, and then dry carbon dioxide was passed over the powder for 6 hours, the temperature being raised from 150° to 200° during the first 3 hours. The product was dissolved in water (1 l.) and shaken with ether, and the precipitate obtained by acidification was collected and recrystallised from water (5 l.), giving *p*-cresotic acid (77·6 g.), m. p. 150° (lit., m. p. 152°).

Action of Heat on O-*Acetyl*-p-*cresotic Acid* (cis-*Di*-p-*cresotide and Tri*-p-*cresotide*).—The thermal decomposition of *O*-acetyl-*p*-cresotic acid (25 g.) was carried out as in previous cases. The crude

sublimate (14·5 g.), which was a mixture, was washed with cold chloroform (50 c.c.), and the compound which was present as large crystals was collected before complete dissolution occurred. This crude material (2·95 g.; m. p. 231—233°) was crystallised 3 times from benzene (60 c.c.) and gave *cis*-di-*p*-cresotide (2·0 g.) as colourless plates, m. p. 235—235·5° (decomp.) (Found: C, 71·8; H, 4·7. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%).

The chloroform filtrate was washed with 5% sodium hydroxide and dried ($MgSO_4$), and then gave a residue (7·8 g.) which was crystallised from benzene (70 c.c.). The crystals (4·8 g.; m. p. 196—200°) were dissolved in hot benzene (150 c.c.), and two main fractions separated (*A*, 2·1 g., m. p. 208—229°; *B*, 1·5 g., m. p. 200—220°). Fraction *A* was washed with cold chloroform, the more slowly dissolving *cis*-di-*p*-cresotide (0·3 g.) collected, and the chloroform removed from the filtrate, giving a residue (1·6 g.) which was combined with fraction *B*. These combined fractions were freed from *cis*-di-*p*-cresotide by refluxing them twice with 95% aqueous acetic acid (50 c.c.), and the crystalline product (1·1 g.; m. p. 244—244·5°) which separated on cooling was recrystallised 3 times from benzene (20 c.c.), giving tri-*p*-cresotide (0·8 g.) as colourless rhombs, m. p. 244·5—245°, containing benzene of crystallisation. This material gave a positive Ramsden's test for benzene, and when heated at 100°/1 mm. gave white pseudomorphic *tri*-p-*cresotide*, m. p. 244·5—245° (Found: C, 71·4; H, 4·4. $C_{24}H_{18}O_6$ requires C, 71·6; H, 4·5%).

Reaction of p-*Cresotic Acid with Phosphorus Oxychloride in Toluene* (*Tetra*-p-*cresotide*).—A mixture of *p*-cresotic acid (50 g.), re-distilled phosphorus oxychloride (50·5 g.), and dry toluene (100 c.c.) was heated on a steam-bath for 11 hours, and after 30 hours was poured on ice-water (200 c.c.). The precipitate was collected, washed with 5% sodium hydroxide, then with water, and dried, yielding a white crystalline solid (38·7 g.; m. p. 285—295°). This was washed with cold chloroform (100 c.c.) and recrystallised twice from chloroform (1 l.)–light petroleum (b. p. 60—80°; 400 c.c.), giving *tetra*-p-*cresotide* (21·3 g.) as colourless hexagonal prisms, m. p. 347° (decomp.) (Found: C, 71·4; H, 4·6. $C_{32}H_{24}O_8$ requires C, 71·6; H, 4·5%).

Alkaline Hydrolysis of the Cresotides.—Method (a). The cresotide (50 mg.) was heated on the steam-bath with 5% aqueous sodium hydroxide solution (4 c.c.) till complete dissolution occurred. Acidificaton gave the corresponding cresotic acid (*o*-cresotic acid, m. p. 163—164°; *m*-cresotic acid, m. p. 176—177°; *p*-cresotic acid, m. p. 150°), identified by mixed m. p.s. The times required for complete dissolution were: *cis*-di-*o*-cresotide, 1 hour (94%); *cis*-di-*m*-cresotide, ½ hour (92%); tri-*m*-cresotide, 5½ hours (91%); *cis*-di-*p*-cresotide, 1½ hours (94%); tri-*p*-cresotide, 96 hours (65%). The percentages given in parentheses are the yields of the cresotic acids.

Method (b). The cresotide (100 mg.) was heated under reflux with 5% *n*-amyl-alcoholic sodium hydroxide (7 c.c.) for the times given below. The amyl alcohol was removed under reduced pressure, water (5 c.c.) added to the residue, and the solution again evaporated under reduced pressure. The residue was dissolved in water, the solution filtered and acidified, and the precipitate collected and recrystallised from water. The reaction times were: tetra-*m*-cresotide, 3 days (80%); hexa(?)-*m*-cresotide, 5 days (80%); tetra-*p*-cresotide, 5 days (95%).

Where the hydrolysis required long heating, the use of glass apparatus caused difficulties in the isolation of the cresotic acids. In the following cases hydrolysis was carried out at 100° in nickel vessels with, initially 70%, sodium hydroxide. The times used were: tri-*o*-cresotide, 7 days (79%); tetra-*o*-cresotide, 6 days (86%).

Molecular Weights of the Cresotides.—These determinations were carried out as described in Part II, and after each determination the solute was recovered unchanged.

The authors' thanks are offered to Monsanto Chemicals, Ltd., for a gift of *m*-cresotic acid. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

THE UNIVERSITY, BRISTOL. [*Received, September 28th*, 1950.]

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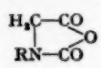
44. *Anhydro-N-carboxyamino-acids. A Friedel–Crafts Type Reaction.*

By F. S. STATHAM.

Anhydro-*N*-carboxy-derivatives of glycine and sarcosine react with benzene in the presence of anhydrous aluminium chloride to give ω-amino- and ω-methylamino-acetophenone, respectively. Similarly isatoic anhydride with benzene yields *o*-aminobenzophenone. Anhydro-*N*-carboxy-DL-β-phenylalanine is cyclised to 2-aminoindanone by anhydrous aluminium chloride.

ALTHOUGH the reaction of internal acid anhydrides of the type of succinic and phthalic anhydrides with benzene in the presence of anhydrous aluminium chloride is well known, there is no information of a corresponding reaction between anhydro-*N*-carboxyamino-acids and benzene under similar conditions. It has now been found that three types of anhydro-*N*-carboxyamino-acids will react under Friedel–Crafts conditions with loss of carbon dioxide.

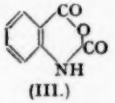
The five-membered anhydro-*N*-carboxy-derivatives of glycine (I; R = H) and sarcosine (I; R = Me) react with benzene in the presence of anhydrous aluminium chloride to give ω-aminoacetophenones (II; R = H and R = Me, respectively) in fair yield.



(I.)

$$PhCO\cdot CH_2\cdot NHR$$

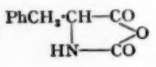
(II.)

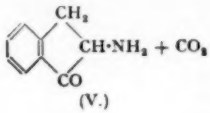


(III.)

Similarly, isatoic anhydride (III) reacts with benzene to give *o*-aminobenzophenone in 30—40% yield.

The effect of aluminium chloride on an anhydro-*N*-carboxy-α-amino-acid containing a phenyl radical, and capable of self-condensation, was also examined. When anhydro-*N*-carboxy-DL-β-phenylalanine (IV) was treated with aluminium chloride in the absence of benzene, cyclisation with loss of carbon dioxide occurred, giving 2-aminoindanone (V) (isolated as picrate) in 54% yield.

(IV.) 



(V.)

Experimental.

When the free amino-ketone was known to be unstable, the yield was estimated from the amount of derivative actually isolated. These figures appear in parentheses after the names of the derivatives prepared.

ω-Aminoacetophenone.—Anhydro-*N*-carboxyglycine (2 g., 0·02 mol.), suspended in methylene dichloride (10 c.c.), was cooled to −10° and powdered aluminium chloride (6 g., 0·045 mol.) was gradually added with stirring. There was no sign of decomposition even on allowing the mixture to warm to 0°; most of the solid material was out of solution. Dry benzene (4 g., 0·5 mol.) was added and the mixture allowed to warm. At 20° vigorous gas evolution began; the temperature was maintained at 10—20° by slight cooling until gas was no longer evolved (2 hours). The reaction mixture was poured on crushed ice (80 g.) containing hydrochloric acid (*d* 1·18; 5 c.c.), filtered, and the methylene dichloride layer separated and discarded. The aqueous layer was extracted three times with ether and divided into portions from which the following derivatives were prepared: Picrate (79%), yellow needles, m. p. (placed in bath at 165°) 174—176° (decomp.), from ethyl alcohol [Goedeckemeyer, *Ber.*, 1888, **21**, 2687, gives m. p. 175° (decomp.)] (Found: N, 15·4. Calc. for $C_8H_9ON,C_6H_3O_7N_3$: N, 15·4%). Platinichloride (67%), m. p. 210—213° (decomp.) with darkening at 200° [Goedeckemeyer, *loc. cit.*, gives m. p. "about 210°" (decomp.)] (Found: N, 3·8; Cl, 31·5; Pt, 28·3. Calc. for $2C_8H_9ON,H_2PtCl_6$: N, 4·1; Cl, 31·2; Pt, 28·5%). Hydrochloride, isolated by saturation of the aqueous layer with gaseous hydrogen chloride at 0° to precipitate inorganic material, filtration of the mixture, and evaporation of the filtrate to dryness; crystallisation of the residue from ethyl alcohol–acetone, gave white needles (56%), m. p. (alone or mixed with an authentic specimen of ω-aminoacetophenone hydrochloride) 185·5° (decomp.), brown at 178°. Benzoyl derivative, m. p. (alone or mixed with an authentic specimen of ω-benzamidoacetophenone) 118—120°.

ω-Methylaminoacetophenone.—Anhydro-*N*-carboxysarcosine (4·6 g.) was mixed with methylene dichloride (20 c.c.), cooled to −10° and, with stirring, powdered aluminium chloride (12 g.) was added. Benzene (8 c.c.) was run in, and the mixture was allowed to warm to room temperature and then stirred overnight. The reaction mass was poured on crushed ice (200 g.), containing concentrated hydrochloric acid (10 c.c.), and extracted with ether. Derivatives of ω-methylaminoacetophenone were prepared from aliquot portions of the aqueous layer as follows: *Picrate* (57%), m. p. (placed in bath at 130°), 143—144° (decomp.) (Found: N, 14·2. $C_9H_{11}ON,C_6H_3O_7N_3$ requires N, 14·3%); recrystallisation from water caused slight decomposition [Gabriel, *Ber.*, 1914, **47**, 1336, gives m. p. 136° (brown at 100°), but no analysis]. Hydrochloride, m. p. 215—217° (decomp.) (Gabriel, *loc. cit.*, gives m. p. 219°) (Found: Cl, 19·1. Calc. for $C_9H_{11}ON,HCl$: Cl, 19·1%). Toluene-*p*-sulphonyl derivative (prepared by using toluene-*p*-sulphonyl chloride and sodium hydrogen carbonate), m. p. 116—118°; repeated crystallisation failed to raise the m. p. (Gabriel, *loc. cit.*, gives m. p. 122°) (Found: N, 4·2. Calc. for $C_{16}H_{17}O_2NS$: N, 4·6%).

2-Aminoindanone.—A suspension of anhydro-*N*-carboxy-DL-β-phenyl-α-alanine (3·8 g.) in methylene dichloride (50 c.c.) was cooled to −10°, and powdered aluminium chloride (6 g.) was added all at once with stirring. The temperature was then allowed to rise to 20° during about 1 hour; at 12°, carbon dioxide was evolved. Stirring was continued at room temperature overnight and then at 40° for a further 5 hours. The reaction mixture was poured on to ice (140 g.)–concentrated hydrochloric acid (10 c.c.), and the majority of the methylene dichloride was separated and discarded. The aqueous layer was filtered to remove a yellow, amorphous solid (1 g.), the filtrate was extracted with ether, and the aqueous layer divided into portions from which the following derivatives of 2-aminoindanone were prepared: Hydrochloride (in poor yield, after removal of inorganic material by precipitation with

gaseous hydrogen chloride), pinkish-white needles from ethyl alcohol–ether; it darkens at 220°, shrinks at 230°, but is not completely molten at 250° (Gabriel and Stelzner, *Ber.*, 1896, **29**, 2606, give decomp. at 230—240°, brown at 200°); it stains filter-paper and the skin a bright bluish-red. Picrate (54%), yellow crystals from chloroform–acetone; it darkens at 140°, is black at 148°, m. p. (placed in bath at 140°) 152° (decomp.) [Gabriel and Stelzner, *loc. cit.*, give m. p. 152° (decomp.)] (Found: N, 14·5. Calc. for $C_9H_9ON,C_6H_3O_7N_3$: N, 14·9%).

o-*Aminobenzophenone*.—An intimate mixture of isatoic anhydride (5·5 g.) and anhydrous aluminium chloride (20 g.) in benzene (30 c.c.) was stirred for 17 hours at laboratory temperature and then at reflux for a further 4·5 hours. Most of the benzene was removed below 60° under reduced pressure, and the residue was poured on ice–hydrochloric acid. The solution was kept overnight, filtered to remove insoluble matter (not further investigated), and the filtrate was made alkaline (Clayton-yellow) with aqueous sodium hydroxide. The precipitated o-aminobenzophenone was extracted into ether, and the extract dried and treated with excess of dry hydrogen chloride to precipitate o-aminobenzophenone hydrochloride, m. p. 178—183° (decomp.) (yield 30% based on isatoic anhydride). When the time of heating under reflux was increased to 8 hours, the yield was increased (43%), but the product was rather less pure, m. p. 172—174° (decomp.). Recrystallisation from acetone raised the m. p. to 186° (decomp.) [Graebe and Ullmann, *Annalen*, 1896, **291**, 14, give m. p. 179—180° (decomp.)] (Found: Cl, 15·2. Calc. for $C_{13}H_{11}ON,HCl$: Cl, 15·2%). The free base crystallised from light petroleum in flat, pale-yellow needles, m. p. 107—108° (Geigy and Königs, *Ber.*, 1885, **18**, 2403, give m. p. 105—106°; Carré, *Bull. Soc. chim.*, 1909, (4), **5**, 280, gives m. p. 110—111°) (Found: N, 7·4. Calc. for $C_{13}H_{11}ON$: N, 7·1%). The acetyl derivative had m. p. 88° (Auwers, *Ber.*, 1896, **29**, 1263, gives m. p. 88·5—89°).

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45. *Substitution Reactions of the Naphthylenediamines. Part I. The Coupling of Diazobenzene to* 1 : 5- *and* 1 : 8-*Naphthylenediamines.*

By J. S. WHITEHURST.

The coupling of diazobenzene to 1 : 5- and 1 : 8-naphthylenediamines has been investigated over a range of pH values and found to occur at position 2 in the former and at position 4 in the latter substance. In almost neutral solution 1 : 8-naphthylenediamine tends to undergo bisazo-coupling. The dissociation constants of naphthalene-1 : 2 : 5- and -1 : 4 : 5-triamines have been determined and compared with those of the diamines from which they are derived.

THE importance of the naphthylenediamines in the dye industry may be judged from the number of patents dealing with their uses. Tetrazotised 1 : 5-naphthylenediamine and its 3 : 7-disulphonic acid yield direct cotton dyes (B.A.S.F., G.P. 39,954, " Friedländer," **1**, 525; Cassella & Co., G.PP. 58,617, 61,174, " Friedländer," **3**, 784), and as a coupled component this diamine has been claimed for the preparation of black acid dyes (Cassella & Co., G.P. 71,329, " Friedländer," **3**, 551). Because 1 : 8-naphthylenediamine was until recently difficult to tetrazotise (Hodgson and Whitehurst, *J.*, 1947, 80), the azo-dyes derived from it were made by using it as a second coupling component (Cassella & Co., G.P. 71,329; B.A.S.F., G.PP. 94,074, 140,955, *Chem. Centr.*, 1898, I, 231; A.-G. f. Anilinf., G.P. 84,657, " Friedländer," **4**, 1022).

The technological use of these compounds has, however, progressed without a fundamental knowledge of their chemistry (see Saunders, " The Aromatic Diazo-Compounds," 2nd edn., 1949, p. 202). For instance, the orientation of diazo-groups when coupled to these diamines has received scant attention. Finzi (*Ann. Chim. Appl.*, 1925, **15**, 55) made a brief study of the coupling reactions with diazotised *p*-toluidine in aqueous hydrochloric acid–sodium acetate and concluded that monocoupling occurred at position 2 in 1 : 5-naphthylenediamine and at position 4 in 1 : 8-naphthylenediamine. Some of the evidence he adduced was of a negative nature, *e.g.*, that the triamine hydrochloride obtained from 1 : 8-naphthylenediamine by coupling and reduction (the intermediates were not crystallised) failed to give a sparingly soluble phenazine with phenanthraquinone. But, as Sachs has shown (*Annalen*, 1909, **365**, 53), ketones can react with the amino-groups of 1 : 8-naphthylenediamine forming perimidines and dihydroperimidines, and these are not necessarily less soluble than the reactants. Finally, Friedländer and Silberstein (*Monatsh.*, 1902, **23**, 518) coupled diazotised sulphanilic acid with 1 : 8-naphthylenediamine, reduced the resulting dye, and then oxidised the products with atmospheric oxygen. Naphthazarin was obtained and as this is now known to be 5 : 8-dihydroxy-1 : 4-naphthaquinone (Dimroth and Ruck, *Annalen*, 1926, **446**, 129) coupling must

have occurred at both positions 4 and 5. The naphthazarin was identified merely by its physical appearance and a few colour reactions, a derivative possessing a melting point not being prepared.

In the present investigation, diazotised aniline was coupled with both 1 : 5- and 1 : 8-naphthylenediamine in aqueous hydrochloric acid–sodium acetate, acetic acid–sodium acetate, pyridine containing calcium carbonate, aqueous ethanol–sodium carbonate, and aqueous ethanol–potassium hydroxide. Under all conditions 1 : 5-naphthylenediamine yielded a mono- and a bis-azo-compound, and as the latter was less soluble in ethanol than the former, a separation was readily effected. The proportion of bisazo-compound increased as the medium became more basic and, as with 1 : 8-naphthylenediamine, an excess of caustic alkali produced intractable tars. Reduction of the monoazo-1 : 5-naphthylenediamine furnished a naphthalenetriamine dihydrochloride (Finzi, *loc. cit.*, describes the formation of a chlorostannate blackened instantly by alkalis) from which a naphthalenetriamine, m. p. 147°, and a tribenzamidonaphthalene, m. p. 282°, were obtained. These compounds would be expected to be 1 : 2 : 5- or 1 : 4 : 5-derivatives. 1 : 4 : 5-Trinitronaphthalene, obtained by nitrating 1 : 5-dinitronaphthalene (de Aguiar, *Ber.*, 1872, **5**, 904; Beilstein and Kuhlberg, *Annalen*, 1873, **169**, 97; Pascal, *Bull. Soc. chim.*, 1920, **27**, 397; Dimroth and Ruck, *loc. cit.*) on reduction and benzoylation yielded 1 : 4 : 5-tribenzamidonaphthalene, m. p. 312°, evidently not identical with the tribenzamidonaphthalene obtained from 1 : 5-naphthylenediamine. Clearly, unless anomalous *meta*-substitution has occurred, the monocoupling of diazobenzene occurs at position 2 over the whole pH range.

The results of coupling diazobenzene with 1 : 8-naphthylenediamine under differing conditions are illustrated qualitatively in Table II (p. 219), and briefly it may be stated that in acid or alkaline solution monocoupling predominated, whilst in acetic acid–sodium acetate the bisazo-compound alone was isolated. It is understandable that attack by the electrophilic coupling reagent on the diamine should be hindered under strongly acid conditions as the diamine will then, in all probability, be doubly protonised, but as the acidity is reduced the degree of protonisation will be lowered and the molecule will become more susceptible to electrophilic attack. With regard to coupling in alkaline media, it would appear that the attacking reagent is not so actively electrophilic as that which functions in neutral or mildly acid circumstances since the diamine can no longer be deactivated by protonisation. A complete explanation cannot be given because of the general obscurity concerning the nature of the coupling entity in alkaline media (Hodgson and Marsden, *J.*, 1945, 207).

Monophenylazo-1 : 8-naphthylenediamine, on reduction, yielded a naphthalenetriamine trihydrochloride, converted by aqueous potassium hydroxide into a crystalline naphthalenetriamine (cf. Finzi, *loc. cit.*). The tribenzoyl derivative of the latter gave no depression of melting point when mixed with an authentic specimen of 1 : 4 : 5-tribenzamidonaphthalene. Thus the monocoupling of diazobenzene to 1 : 8-naphthylenediamine occurs at position 4.

It is of interest to compare these results with the coupling reactions of other similarly constituted naphthalene compounds. According to Heller and Kretzschmann (*Ber.*, 1921, **54**, 1098), 1 : 8-dihydroxynaphthalene gives mono- and bis-azo-compounds, with the azo-links at positions 4 and 5. Apparently no data exist for 8-amino-1-naphthol itself; although its *N*-acetyl compound couples *para* to the hydroxyl group with diazotised aniline (Fichter and Gageur, *Ber.*, 1906, **39**, 3331), the *N*-toluene-*p*-sulphonyl compound produces a mixture of mono- and bis-azo-compounds of undetermined structure (Fichter and Kuhnel, *Ber.*, 1909, **42**, 4748). It is difficult to attach more than one azo-link to 1 : 5-dihydroxynaphthalene, and it couples in position 2 or 4 according to the nature of the diazonium compound and the conditions of coupling. Diazobenzene attacks position 4 (Fischer and Bauer, *J. pr. Chem.*, 1917, **95**, 261) whilst the important dye Diamond Black PV (C.I. 170) is made by the coupling of the diazo-oxide of 2-aminophenol-4-sulphonic acid at position 2. Porai-Koshits *et al.* have more recently made the important discovery that the attack of diazo-compounds on 5-amino-1-naphthol never occurs *para* to the amino-group, the only exception being diazotised H-acid (*J. Gen. Chem. Russia*, 1945, **15**, 446; 1947, **17**, 1758, 1807). It is clear that in the naphthalene series amino-groups have a greater tendency to bring about *ortho*-coupling than have hydroxyl groups.

4-Phenylazo-1 : 8-naphthylenediamine reacted very slowly with boiling 90% formic acid yielding the perimidine, and could only be monoacylated with *p*-toluenesulphonyl chloride in pyridine solution, the product being, most likely, 1-amino-4-phenylazo-8-*p*-toluenesulphonamidonaphthalene. No isolable product was obtained by the action of *p*-toluenesulphonyl chloride on 2-phenylazo-1 : 5-naphthylenediamine in pyridine solution. This was surprising as it might have been reasonably expected that the chelating influence of the azo-

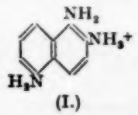
group (Elkins and Hunter, *J.*, 1935, 1598; Hunter, *J.*, 1937, 320) on the one *ortho*-amino-group would have left the other free to react with the acylating agent. Attempts were made, without success, to determine the constitution of the bisazo-1 : 8-naphthylenediamine by reduction and benzoylation. 1 : 4 : 5 : 8-Tetrabenzamidonaphthalene, useful as a possible reference substance for future investigations, was made from 1 : 4 : 5 : 8-tetranitronaphthalene.

The dissociation constants of naphthalene-1 : 2 : 5- and -1 : 4 : 5-triamines were determined by potentiometric titration of their hydrochlorides in 50% aqueous ethanol. The hydrochlorides of 1 : 5- and 1 : 8-naphthylenediamines were titrated in like manner. The results are recorded in Table I. The constants for 1 : 5- and 1 : 8-naphthylenediamines are essentially in agreement with those found by Kuhn and Wassermann (*Helv. Chim. Acta*, 1928, **11**, 79). The discrepancy in the value of pK_2 for 1 : 5-naphthylenediamine is partly caused by the use by these authors of an empirical equation due to Bjerrum (*Z. Elektrochem.*, 1918, **24**, 321; *Z. physikal. Chem.*, 1923, **104**, 406), which is now known to be inaccurate.

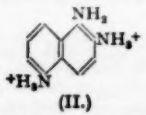
TABLE I.

	(14°).			Kuhn and Wassermann.	
	pK_3.	pK_2.	pK_1.	pK_2.	pK_1.
1 : 5-Naphthylenediamine	—	1·94	4·06	1·74 (19°)	4·07 (20°)
1 : 8-Naphthylenediamine	—	1·49	4·29	—	4·29 (17°)
Naphthalene-1 : 2 : 5-triamine	—	2·61	5·58	—	—
Naphthalene-1 : 4 : 5-triamine	*ca.* 2·4	*ca.* 2·4	5·89	—	—

The greater basicity of β-naphthylamine compounds compared with the corresponding α-compounds probably indicates structures (I) and (II) for the singly and doubly charged cations of naphthalene-1 : 2 : 5-triamine. The low value of K_1 for naphthalene-1 : 4 : 5-triamine ($1·29 \times 10^{-6}$) is near that for 1 : 4-naphthylenediamine ($2·88 \times 10^{-6}$), by far the strongest base



(I.)



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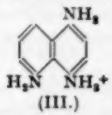

(III.)

among the naphthylenediamines investigated by Kuhn and Wassermann (*loc. cit.*). By analogy the first dissociation constant of naphthalene-1 : 4 : 5-triamine almost certainly involves the 1- or the 4-amino-group. As the second and third dissociation constants have been found to be virtually equal, the protonised amino-group of the singly charged cation must influence the other two amino-groups equally as regards the acceptance of hydrogen ions. A proton situated on the 1-amino-group would be unlikely to do this, and hence the structure of the singly charged cation of naphthalene-1 : 4 : 5-triamine is probably (III).

EXPERIMENTAL.

(M. p.s are uncorrected.)

Dihydrochlorides of 1 : 5- *and* 1 : 8-*Naphthylenediamines.*—Benzene solutions of the pure diamines were treated with an excess of dry hydrogen chloride, and the white sludge was collected, washed with benzene, and dried at 50°. Both products were colourless solids, very soluble in water in contrast to the diamines which dissolve slowly in dilute hydrochloric acid.

Coupling of Diazobenzene to 1 : 5-*Naphthylenediamine.*—(a) *In aqueous hydrochloric acid–sodium acetate.* The diamine dihydrochloride (1·50 g.) in water (200 c.c.) was treated at 0° with benzenediazonium chloride [from 0·63 g. of aniline and 1·60 c.c. of hydrochloric acid (*d* 1·18), the solution having been freed from nitrous acid with urea]. Sodium acetate (10 g.) in water (100 c.c.) was then added at 0° with stirring, and after 1 hour the deep-red precipitate was collected, washed, and dried (1·5 g.). Crystallisation from ethanol yielded the less soluble *bisazo*-derivative (0·10 g.), which formed deep red needles, m. p. 240° (decomp.) (Found : C, 72·3; H, 5·1; N, 22·6. $C_{22}H_{18}N_6$ requires C, 72·1; H, 5·0; N, 22·9%), and the more soluble *monoazo*-derivative (0·94 g.), which separated in red needles, m. p. 148° (Found : C, 73·6; H, 5·5; N, 21·2. $C_{16}H_{14}N_4$ requires C, 73·3; H, 5·4; N, 21·4%).

The monoazo-compound imparted an orange-red colour to concentrated sulphuric acid, which changed to purplish-red in thin films and to pale orange on dilution with water. The bisazo-derivative gave a beautiful claret colour with the same reagent, turning to purplish-green in thin films and to blue on dilution with water.

(b) *In acetic acid–sodium acetate.* The addition of a nitrous acid-free solution of benzenediazonium chloride [from 0·61 g. of aniline and 1·60 c.c. of hydrochloric acid, *d* 1·18)] to a well stirred solution of the diamine (1 g.) in glacial acetic acid (125 c.c.), followed by the addition of sodium acetate (10 g.) in water (100 c.c.) at 0° and then 10% aqueous potassium hydroxide (*ca.* 200 c.c.), gave a precipitate of

azo-compounds, which, crystallised from ethanol as above, gave the same amounts of mono- and bis-azo-derivatives.

(c) *In pyridine containing calcium carbonate.* 1 : 5-Naphthylenediamine (1 g.) in pyridine (80 c.c.) containing powdered calcium carbonate (1·5 g.) was treated at 0°, with stirring, with a solution of benzenediazonium chloride (from 0·62 g. of aniline, the solution having been freed from nitrous acid with urea and made neutral with calcium carbonate). After filtration, water (*ca.* 80 c.c.) was added to the solution, and the red crystalline precipitate which had a marked green reflex was collected (0·44 g.) and crystallised from ethanol. The bisazo-derivative separated in deep red needles (0·24 g.). Further addition of water (*ca.* 200 c.c.) to the pyridine solution precipitated the crude monoazo-compound (0·48 g.) which crystallised from ethanol in rosettes of needles (0·22 g.).

(d) *In aqueous ethanolic potassium hydroxide.* The diamine (1 g.) in ethanol (200 c.c.) containing sufficient potassium hydroxide to neutralise the mineral acid liberated in coupling, when treated with either one or two moles of benzenediazonium chloride, gave difficultly crystallisable mixtures of mono- and bis-azo-compounds.

Reduction of the Monoazo-compound.—The compound (0·70 g.) in ethanol (30 c.c.) was reduced, at 80°, with stannous chloride (1·75 g.) in *ca.* 12 c.c. of fuming hydrchloric acid. On cooling, the white precipitate of the *triamine dihydrochloride* (0·45 g.) was removed, washed with a little ethanol, and dried in a vacuum. A portion was crystallised by dissolution in the minimum quantity of aqueous ethanol and addition of alcoholic hydrogen chloride cautiously until precipitation of the colourless needles commenced (Found: C, 48·7; H, 5·5; N, 16·2; Cl, 27·4. $C_{10}H_{13}N_3Cl_2$ requires C, 48·8; H, 5·3; N, 17·1; Cl, 28·8%).

When the compound in a minimum quantity of water was treated cautiously with 20% potassium hydroxide solution at 0° it gave a colourless crystalline precipitate of *naphthalene*-1 : 2 : *5-triamine*, m. p. 147° (Found: C, 68·7; H, 6·7; N, 24·0. $C_{10}H_{11}N_3$ requires C, 69·3; H, 6·4; N, 24·2%). Attempted crystallisation of this substance from ethanol gave a product less pure than the original material. Treatment of the hydrochloride with benzoyl chloride and aqueous potassium hydroxide gave the *tribenzoyl* derivative, which, though sparingly soluble, crystallised from glacial acetic acid in colourless needles, m. p. 282° (Found: C, 76·2; H, 5·0; N, 8·1. Calc. for $C_{31}H_{23}O_3N_3$: C, 76·7; H, 4·8; N, 8·7%) (Finzi, *loc. cit.*, gives m. p. 268°). The compound gave no depression of melting point when mixed with an authentic specimen of 1 : 4 : 5-tribenzamidonaphthalene, m. p. 312°, but the mixture decomposed with bubbling at 282°.

The triamine dihydrochloride (0·2 g.) was treated with toluene-*p*-sulphonyl chloride (0·44 g.) in hot (95°) pyridine. After 3 hours, dilution with water gave a precipitate which, crystallised repeatedly from ethanol (charcoal), gave a small yield of colourless crystalline material (needles), m. p. 145—155°, which analysed satisfactorily for 1 : 2 : *5-tritoluene-p-sulphonamidonaphthalene* (Found: C, 57·6; H, 4·8. $C_{31}H_{29}O_6N_3S_3$ requires C, 58·6; H, 4·6%). The reaction between toluene-*p*-sulphonyl chloride and naphthalene-1 : 2 : 5-triamine dihydrochloride in aqueous sodium carbonate gave a similar product.

Coupling of Diazobenzene to 1 : 8-*Naphthylenediamine.*—Experiments, summarised in Table II, are considered in more detail below. 4-*Phenylazo*-1 : 8-*naphthylenediamine. Method A* (*a*). 1 : 8-Naphthylenediamine dihydrochloride (1·27 g.) in water (150 c.c.) was treated with a nitrous acid-free solution of benzenediazonium chloride, prepared from aniline (0·5 g.), hydrochloric acid (1·25 c.c.; *d* 1·18), and sodium nitrite (0·45 g.) in a minimum of water at 0°. A blue-violet colour developed but no precipitate appeared until sodium acetate (7·5 g.) in water (*ca.* 50 c.c.) was added. The red solid was collected, washed well with water and dilute aqueous ammonia, and dried in a vacuum (1·2 g.). It was dissolved in ethanol containing a few drops of ammonia (*d* 0·880) and water added until crystallisation commenced (1·03 g.). Recrystallisation from aqueous ethanol furnished light-scarlet plates of 4-*phenylazo*-1 : 8-*naphthylenediamine* (0·75 g.), m. p. 115° (Found: C, 73·1; H, 5·4; N, 21·2. $C_{16}H_{14}N_4$ requires C, 73·3; H, 5·4; N, 21·4%). The compound was soluble in most organic solvents, and very soluble in ether. It imparted an orange-yellow colour to concentrated sulphuric acid, which changed to violet-pink in thin films or on dilution with water.

Method B (*c*). The diamine (1·58 g.) in glacial acetic acid (150 c.c.) was treated with a neutral, nitrous acid-free solution of benzenediazonium chloride [from 0·93 g. of aniline, 2·40 c.c. of hydrochloric acid (*d* 1·18), and 0·75 g. of sodium nitrite in 12 c.c. of water]. Sodium acetate (7·5 g.) in water (100 c.c.) was then added with stirring. The violet precipitate (1·04 g.) was then worked up as described above.

Method B (*e*). This method was similar to *B* (*c*) except that conditions were kept as nearly anhydrous as possible, the sodium acetate (1·1 g.) being dissolved in the diamine–glacial acetic acid solution before the rapid addition of the benzenediazonium chloride solution. 4-*Phenylazo*-1 : 8-*naphthylenediamine monohydrochloride* separated from the solution in deep red needles possessing a green metallic lustre (m. p. >360°). It was extracted with boiling ethanol and dried (1·1 g.) (Found: C, 64·1; H, 5·2; N, 18·8; Cl, 12·0. $C_{16}H_{15}N_4Cl$ requires C, 64·3; H, 5·1; N, 18·8; Cl, 11·9%). The same compound was formed from the azo-compound and dry hydrogen chloride in glacial acetic acid solution.

Method D (*j*). A neutral nitrous acid-free solution of benzenediazonium chloride (from 0·93 g. of aniline) was added slowly to a vigorously stirred solution of 1 : 8-naphthylenediamine (1·58 g.) in 80% ethanol (400 c.c.) containing sodium carbonate (7 g.) at *ca.* 10°. The solution was then warmed to *ca.* 60° and water (*ca.* 300 c.c.) added until the red plates began to separate. Crystallisation from ethanol containing a few drops of aqueous ammonia (*d* 0·880) gave scarlet plates of 4-phenylazo-1 : 8-naphthylenediamine (1·02 g.; m. p. 115°).

The bisazo-compound. Method B (*d*). The procedure was similar to that of method *B* (*c*) except that the benzenediazonium chloride solution (2 moles), rendered free from nitrous acid with urea and from mineral acid with calcium carbonate, was run at 0° into the diamine (1·58 g.) in glacial acetic acid

(150 c.c.), to which sodium acetate (7·5 g.) in water (30 c.c.) had been added. The dark-violet precipitate was collected, washed, dried (vacuum), and crystallised four times from ethanol. The *bisphenylazo-1 : 8-naphthylenediamine* formed dark red needles (0·24 g.; m. p. 195°) (Found : C, 71·9; H, 5·1; N, 22·8. $C_{22}H_{18}N_6$ requires C, 72·1; H, 5·0; N, 22·9%). It was less soluble than the monoazo-derivative and gave a dark brown colour with concentrated sulphuric acid, becoming purplish-green in thin films and deep blue on dilution with water.

TABLE II.

	Diamine, moles.	PhN_2Cl, moles.	NaOAc, moles.	Mode of mixing.	Chief product.
Method A. 1 : 8-Naphthylenediamine dihydrochloride in water–benzenediazonium chloride–sodium acetate.					
(*a*)	1	1	10	Sodium acetate solution added to mixture of diamine and PhN_2Cl	Monoazo-compound
(*b*)	1	1	10	Diazonium solution run into diamine and sodium acetate	Bisazo-compound
Method B. 1 : 8-Naphthylenediamine in acetic acid–benzenediazonium chloride–sodium acetate.					
(*c*)	1	1	10	Sodium acetate added to diamine and PhN_2Cl	Monoazo-compound
(*d*)	1	1	10	Diazonium solution run into diamine–sodium acetate–acetic acid solution	Bisazo-compound
(*e*)	1	1	1½	Similar to (*d*). Rapid addition of diazonium solution	Monoazocompound monohydrochloride
(*f*)	1	2	6	Similar to (*d*)	Bisazo-compound
Method C. 1 : 8-Naphthylenediamine in pyridine containing calcium carbonate treated with a neutral solution of benzenediazonium chloride.					
(*g*)	1	1	—	—	Bisazo-compound
(*h*)	1	2	—	—	Bisazo-compound
(*i*)	1	3	—	—	Bisazo-compound
Method D. A neutral solution of benzenediazonium chloride added to an aqueous ethanolic solution of 1 : 8-naphthylenediamine containing sodium carbonate.					
(*j*)	1	1	—	—	Monoazo-compound
Method E. A neutral solution of benzenediazonium chloride added to an ethanol solution of 1 : 8-naphthylenediamine containing sufficient potassium hydroxide to permit the maximum degree of coupling.					
(*k*)	1	1	—	—	Monoazo-compound
(*l*)	1	2	—	—	Monoazo-compound
(*m*)	1	3	—	—	No cryst. product isolated

Reduction of 4-Phenylazo-1 : 8-naphthylenediamine.—The compound (1 g.) in hot ethanol (50 c.c.) was reduced with stannous chloride (3·5 g.) in fuming hydrochloric acid (20 c.c.). The initial violet precipitate became colourless and the crystalline *triamine trihydrochloride* (0·72 g.) was collected on cooling. A portion was crystallised from aqueous ethanol by adding alcoholic hydrogen chloride. The compound formed colourless needles (Found : C, 43·0; H, 5·0; N, 14·4; Cl, 36·8. $C_{16}H_{14}N_3Cl_3$ requires C, 42·5; H, 5·0; N, 14·9; Cl, 37·6%). 10% Sodium hydroxide solution furnished the crystalline *triamine*, m. p. 156° (Found : C, 69·0; H, 6·4; N, 23·5. $C_{16}H_{17}N_3$ requires C, 69·3; H, 6·4; N, 24·2%), which rapidly became oxidised when moist but was quite stable when dry.

The *tribenzoyl* derivative was made by treating the triamine hydrochloride (0·5 g.) with benzoyl chloride in dilute potassium hydroxide solution. The yellow residue (0·87 g.) crystallised from glacial acetic acid in colourless needles, m. p. 312° (Found : C, 76·7; H, 5·1; N, 8·1. $C_{31}H_{23}O_3N_3$ requires C, 76·7; H, 4·8; N, 8·7%).

1 : 4 : 5-*Tritoluene-p-sulphonamidonaphthalene* was obtained from the triamine hydrochloride (0·3 g.) and toluene-*p*-sulphonyl chloride (0·78 g.) in hot pyridine. The solid was precipitated with dilute hydrochloric acid and several crystallisations from ethanol (charcoal) gave crystalline material, m. p. *ca.* 150°, raised to 248° by two further crystallisations from toluene, in which the *compound* is only sparingly soluble (0·057 g.) (Found : C, 58·1; H, 4·6. $C_{31}H_{29}O_6N_3S_3$ requires C, 58·6; H, 4·6%).

6(7)-Phenylazoperimidine was made by refluxing 4-phenylazo-1 : 8-naphthylenediamine (0·2 g.) with 90% formic acid (10 c.c.) for 3 hours. The solution was poured into water and rendered alkaline with aqueous ammonia, and the scarlet gelatinous precipitate collected. It crystallised from ethanol with some difficulty, forming small prisms, darkening and decomposing continuously above 180° (Found : N, 20·2. $C_{17}H_{12}N_4$ requires N, 20·6%). The compound gave a vivid blue-green colour with concentrated sulphuric acid.

1-*Amino-4-phenylazo-8-toluene-p-sulphonamidonaphthalene* was prepared by heating together 4-phenylazo-1 : 8-naphthylenediamine (0·17 g.), pyridine (7 c.c.), and toluene-*p*-sulphonyl chloride (0·1 g.) on the water-bath for 2 hours. Addition of water gave a dark red precipitate which, after extraction with hot ethanol, crystallised from pyridine in dark red, very small needles, m. p. 238° (Found :

C, 65·9; H, 4·8; N, 13·7. $C_{22}H_{18}O_3N_4S$ requires C, 66·3; H, 4·8; N, 13·5%). Attempts to prepare the ditoluene-*p*-sulphonyl derivative failed, both in pyridine solution and in hot aqueous sodium carbonate suspension.

1 : 4 : 5-*Trinitronaphthalene.*—The methods described by de Aguiar, and Beilstein and Kuhlberg (*locc. cit.*), gave considerable amounts of 1 : 4 : 5 : 8-tetranitronaphthalene, which hindered the purification of the trinitro-compound. That of Dimroth and Ruck (*loc. cit.*) was satisfactory but inconvenient and the following was adopted. 1 : 5-Dinitronaphthalene (5 g.) was stirred into sulphuric acid (100 c.c.; *d* 1·84) and nitric acid (20 c.c.; *d* 1·42) was added slowly. The dinitro-compound dissolved and the trinitronaphthalene was precipitated. After 30 minutes it was collected on sintered glass, washed, dried, and crystallised from benzene. 1 : 4 : 5-Trinitronaphthalene separated in long yellow needles (1·84 g.), m. p. 149°, the surface of which sintered on evaporation of the solvent (Found : C, 45·5; H, 1·9; N, 16·0. Calc. for $C_{10}H_5O_6N_3$: C, 45·6; H, 1·9; N, 16·0%) (de Aguiar, *loc. cit.*, gives m. p. 154°; Dimroth and Ruck, *loc. cit.*, give m. p. 148—149°; Desvergnes, *Monit. Scient.*, 1926, **16**, 73, gives m. p. 147·8—148·3°).

FIG. 1.

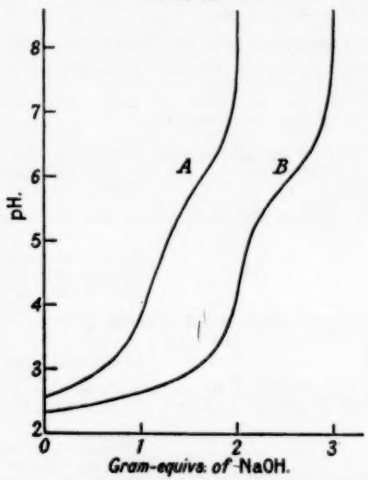

FIG. 2.

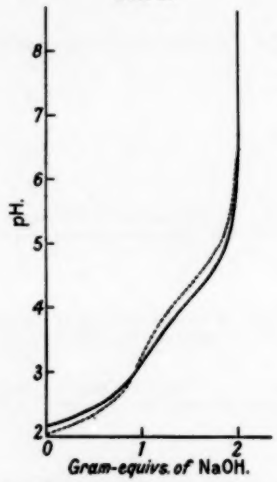

FIG. 1. A, *Naphthalene-*1 : 2 : 5-*triamine dihydrochloride* (38·2 *mg.*) *in* 50% (*v*/*v*) *ethanol* (20 *c.c.*).
B, *Naphthalene-*1 : 4 : 5-*triamine trihydrochloride* (35·4 *mg.*) *in* 50% (*v*/*v*) *ethanol* (20 *c.c.*).

FIG. 2. ———, 1 : 5-*Naphthylenediamine dihydrochloride* (69·9 *mg.*) *in* 50% (*v*/*v*) *ethanol* (20 *c.c.*).
– – – –, 1 : 8-*Naphthylenediamine dihydrochloride* (63·5 *mg.*) *in* 50% (*v*/*v*) *ethanol* (20 *c.c.*).
Hydrogen was bubbled through the solutions during the titrations.

Reduction of 1 : 4 : 5-*Trinitronaphthalene.*—The compound (1·5 g.) was warmed with ethanol (300 c.c. on the water-bath, and a solution of stannous chloride (14 g.) in fuming hydrochloric acid (45 c.c.) was added. The deep orange-coloured solution, on evaporation under reduced pressure in a stream of hydrogen, gave colourless crystals of a *stannichloride*, in which the triamine was presumably monoacidic (Found : Cl, 31·1, 31·4. $2C_{10}H_{11}N_3,H_2SnCl_6$ requires Cl, 31·3%) but the addition of concentrated hydrochloric acid or preferably ethanolic hydrogen chloride precipitated the triamine trihydrochloride (1·29 g.) (Found : C, 41·9; H, 5·1%). Basification gave the triamine, m. p. 156°, and the action of benzoyl chloride and aqueous potassium hydroxide on the latter produced 1 : 4 : 5-tribenzamidonaphthalene, m. p. 312° (Found : C, 76·0; H, 5·0. $C_{31}H_{23}O_3N_3$ requires C, 76·7; H, 4·8%).

1 : 4 : 5 : 8-*Tetrabenzamidonaphthalene.*—1 : 4 : 5 : 8-Tetranitronaphthalene (Will, *Ber.*, 1895, **28**, 367; Dimroth and Ruck, *loc. cit.*) was made by dinitrating 1 : 5-dinitronaphthalene. The latter (10 g.) was dissolved in nitric acid (100 c.c.; *d* 1·52) and sulphuric acid (100 c.c.; *d* 1·84) was added slowly at *ca.* 80°. After 30 minutes, ice was added to the solution until a crystalline precipitate appeared, which was collected on sintered glass, washed, and extracted with a little cold acetone. The residue (4·2 g.) was crystallised from nitrobenzene. 1 : 4 : 5 : 8-Tetranitronaphthalene (2·9 g.) formed pale yellow needles, darkening at *ca.* 280° and melting on rapid heating at *ca.* 340° (decomp.) (Found : C, 39·5; H, 1·3; N, 18·9. Calc. for $C_{10}H_4O_8N_4$: C, 39·0; H, 1·3; N, 18·2%) [Dimroth and Ruck, *loc. cit.*, give m. p. 340—345° (decomp.)].

The nitro-compound (0·5 g.) was heated under reflux with granulated tin (1·5 g.), hydrochloric acid (15 c.c.; *d* 1·18), and water (5 c.c.). After 1 hour the orange-brown solution was filtered, water (20 c.c.) was added, the solution was saturated with hydrogen sulphide, and the precipitated tin sulphides were removed. The solution was then evaporated under hydrogen at reduced pressure, neutralised with dilute potassium hydroxide solution (phenolphthalein), and poured into an emulsion of benzoyl chloride

in dilute sodium carbonate solution. After 6 hours at 0°, the solution was acidified with dilute hydrochloric acid and filtered, and the residue was then extracted with warm (35°) dilute potassium hydroxide solution. Crystallisation from ethanol (charcoal) gave colourless prisms of 1 : 4 : 5 : 8-*tetrabenzamidonaphthalene* (0·023 g.), m. p. 233° (Found : C, 76·0; H, 4·0. $C_{34}H_{28}O_4N_4$ requires C, 75·5; H, 4·7%).

Bisphenylazo-1 : 8-naphthylenediamine (0·5 g.) was reduced with stannous chloride in aqueous ethanolic hydrogen chloride; the solution, added to a mixture of benzoyl chloride–aqueous potassium hydroxide at 0°, gave a product (0·7 g.), which on crystallisation from ethanol furnished benzanilide, m. p. 161°, alone and mixed with an authentic specimen.

Potentiometric Titration.—The cell employed was a glass electrode–calomel electrode system, the E.M.F. being measured by a Cambridge pH-meter. The glass electrode was first calibrated with solutions of known pH. The amine hydrochlorides were dissolved in 50% (v/v) air-free ethanol, and titrated with 0·1N-sodium hydroxide solution (carbonate-free) in an atmosphere of hydrogen at 14°. The results are shown graphically in Figs. 1 and 2. For the subsequent calculations, equations due to Britton ("Hydrogen Ions," London, Chapman and Hall, 1932, p. 198; cf. Noyes, *Z. physikal. Chem.*, 1893, **11**, 495) were employed. For the diacidic amines the ionic equilibria are

$$R(NH_2)(NH_3^+) \rightleftharpoons R(NH_2)_2 + H^+$$
$$R(NH_3^+)_2 \rightleftharpoons R(NH_2)(NH_3^+) + H^+$$

with dissociation constants $K_1 = \dfrac{[R(NH_2)_2][H^+]}{[R(NH_2)(NH_3^+)]}$ and $K_2 = \dfrac{[R(NH_2)(NH_3^+)][H^+]}{[R(NH_3^+)_2]}$ respectively.

If c = total concentration of the diamine, a = total concentration of the added alkali, and h = hydrogen ion concentration, then for any point on the titration curve parameters A, B, and D are given by $A = h(a + h - c)$; $B = 2c - (a + h)$; $D = h^2(a + h)$, and the dissociation constants by the expressions

$$K_1 = \frac{A_1D_2 - A_2D_1}{B_1D_2 - B_2D_1} \text{ and } K_2 = \frac{B_1D_2 - B_2D_1}{A_1B_2 - A_2B_1}.$$

Activity coefficients were not used in the calculations as at the dilution of the solutions under observation they would be approximately unity. In determining the three dissociation constants of 1 : 4 : 5-naphthalenetriamine, the shape of the pH titration curve made it obvious that the Henderson equation (*J. Amer. Chem. Soc.*, 1908, **30**, 954) was applicable, without serious error, over the last-third portion of the curve in order to evaluate K_1. K_2 and K_3 $\left\{= \dfrac{[R(NH_2)(NH_3^+)_2][H^+]}{[R(NH_3^+)_3]}\right\}$ were then determined by applying the Britton equations over the first-two-thirds portion of the curve.

The author gladly acknowledges Dr. H. H. Hodgson's permission further to develop investigations carried out with him at Huddersfield during 1943—44 and thanks him for his interest in this work. The author is grateful to Professor H. T. S. Britton for valuable discussions on the potentiometric work, and to Dr. K. Schofield for helpful criticism. Acknowledgment is made to the Council of the University College, Exeter, and Imperial Chemical Industries Limited for financial aid.

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46. *Substitution Reactions of the Naphthylenediamines. Part II. The Bromination of the Ditoluene-*p*-sulphonyl Derivatives of* 1 : 5- *and* 1 : 8-*Naphthylenediamines.*

By J. S. WHITEHURST.

Bromination of the compounds named in the title has been studied under various conditions. 1 : 5-Ditoluene-*p*-sulphonamidonaphthalene has yielded a 4 : 8-dibromo-, and 1 : 8-ditoluene-*p*-sulphonamidonaphthalene a 4-monobromo-derivative. The constitution of these compounds has been established by unequivocal methods. Bromination of 1 : 5-dibromonaphthalene gives a tetrabromonaphthalene identical with that prepared by brominating 1 : 5- and 1 : 8-dinitronaphthalenes. This compound is not 1 : 4 : 5 : 8-tetrabromonaphthalene.

NITRATION of the ditoluene-*p*-sulphonyl derivatives of 1 : 5- and 1 : 8-naphthylenediamines has been previously reported and in each case tetranitro-compounds are produced (Hodgson and Whitehurst, *J.*, 1947, 80). The present paper deal with the bromination and subsequent nitration of these compounds.

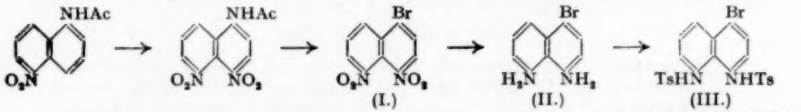
1 : 5-Ditoluene-*p*-sulphonamidonaphthalene did not undergo bromination in chloroform, but in glacial acetic acid it gave a dibromo-derivative, hydrolysed slowly by means of

concentrated sulphuric acid to a dibromonaphthylenediamine. Tetrazotisation and deamination of the latter furnished a dibromonaphthalene, having identical properties and giving no depression of melting point with an authentic specimen of 1 : 5-dibromonaphthalene, prepared unequivocally from 1 : 5-naphthylenediamine by the Sandmeyer reaction. Clearly, 1 : 5-ditoluene-*p*-sulphonamidonaphthalene undergoes bromination at the 4 : 8-positions. From the dibromonaphthylenediamine, by the usual methods, were prepared the corresponding 4 : 8-dibromo-1 : 5-dichloro-, 1 : 4 : 5 : 8-tetrabromo-, and 1 : 5-dibromo-4 : 8-di-iodonaphthalenes. The tetrabromonaphthalene thus obtained, m. p. 145°, was obviously not identical with that, m. p. 308°, described by Dhar (*J.*, 1920, 997) as the 1 : 4 : 5 : 8-compound, which had been made by the action of bromine on either 1 : 5- or 1 : 8-dinitronaphthalene. In view of this, it was decided to repeat Dhar's work.

It was found that either 1 : 5- or 1 : 8-dinitronaphthalene on being heated with two moles of bromine yielded a tetrabromonaphthalene, m. p. 231°. The best yield was obtained from 1 : 5-dinitronaphthalene and, even after prolonged heating, this compound still gave a good yield of the same tetrabromonaphthalene. Zalkind and Belikov (*Ber.*, 1931, **64**, 955) have reported a tetrabromonaphthalene, m. p. 235°, among the bromination products of 1 : 5-dibromonaphthalene and we confirmed their results; the tetrabromonaphthalene, m. p. 231°, gave no depression of melting point with that obtained previously. Dhar's formula rests on two postulates: first, that a bromine atom replaces a nitro-group, and as identical compounds are obtained from 1 : 5- and 1 : 8-dinitronaphthalenes three of the bromine atoms must be in the 1 : 4 : 5-positions, and secondly, that the remaining α-carbon atom is more readily attacked than any other. Neither assumption is necessarily correct. Zalkind and Belikov (*loc. cit.*) have established that the tribromonaphthalene obtained by brominating 1-bromonaphthalene is the 1 : 4 : 6-compound and, although, in their experiments, the bromination of 1 : 5-dibromonaphthalene was not arrested at the tribromo-stage, it is quite probable that 1 : 4 : 6-tribromonaphthalene is a precursor of the tetrabromonaphthalene described here, which may be 1 : 4 : 6 : 8-tetrabromonaphthalene.

Nitration of 4 : 8-dibromo-1 : 5-ditoluene-*p*-sulphonamidonaphthalene in glacial acetic acid gave 4-bromo-2 : 6 : 8-trinitro-1 : 5-ditoluene-*p*-sulphonamidonaphthalene, replacement of a bromine atom by a nitro-group having occurred. An attempted synthesis of this compound from 5-nitro-1-toluene-*p*-sulphonamidonaphthalene by bromination and subsequent reduction, toluenesulphonation, and nitration proved unsuccessful as the compound yielded a mixture of isomeric monobromo-derivatives from which the required 4-bromo-5-nitro-1-toluene-*p*-sulphonamidonaphthalene was isolated in too poor a yield for further work. It is an interesting comparison that 5-nitro-1-naphthylamine undergoes bromination in the 2-position in good yield (Hodgson and Turner, *J.*, 1942, 723).

Bromine reacted with 1 : 8-ditoluene-*p*-sulphonamidonaphthalene in chloroform or glacial acetic acid yielding, somewhat surprisingly, a monobromo-derivative, m. p. 208°. Hydrolysis of this compound could not be effected with sulphuric, hydrochloric, or phosphoric acid. Unless *meta*-substitution had occurred, the substance must have been either 2- or 4-bromo-1 : 8-ditoluene-*p*-sulphonamidonaphthalene, and according to Hodgson and Hathway (*J.*, 1945, 543) the latter (m. p. 225°) is preparable by the sequence of reactions:



(I.) (II.) (III.)

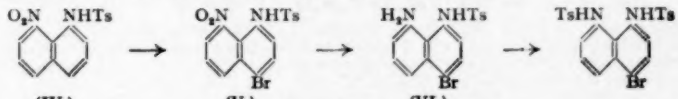
(Ts = *p*-$C_6H_4Me{\cdot}SO_2$)

As a means of obtaining (I) the synthesis is costly, and in our work the nitration of 1-bromonaphthalene (Merz and Weith, *Ber.*, 1882, **15**, 2708) was found to be more practicable. Reduction of (I) according to the directions of Hodgson and Hathway (*loc. cit.*) could not be achieved, but (I) did undergo reduction with stannous chloride in glacial acetic acid–hydrogen chloride, the stannichloride of (II) being obtained in fair yield. From it the hydrochloride and sulphate were prepared. An interesting feature of these salts is that the diamine behaves as a monoacidic base (cf. Hodgson and Hathway, *loc. cit.*, who give the normal formula for the sulphate). These findings were established not only by elementary analysis but also by conductometric and potentiometric titrations. Evaporation of ethereal or benzene solutions of the free diamine at reduced pressure under hydrogen gave pale green glassy solids which could not be induced to crystallise. Advent of moisture or air caused a fairly rapid coloration to

brown and then green, and an alcoholic solution of the diamine, even in the absence of oxygen, deposited a green amorphous powder stable on heating to 300°. The unstable nature of halogenonaphthylenediamines appears characteristic: for instance, 4 : 8-dibromo-1 : 5-naphthylenediamine explodes at 115°, and with hot ethanol is transformed into amorphous blue products; also, 4-chloro-1 : 8-naphthylenediamine (B.A.S.F., G.P. 122,475) is known only as its sulphate.

The action of toluene-*p*-sulphonyl chloride and sodium carbonate on a benzene solution of (II) (Hodgson and Hathway, *loc. cit.*) gave, in one experiment, a small amount (insufficient for analysis) of crystalline material, m. p. 215° (decomposing at 218°), which depressed the melting point of the bromination product of 1 : 8-ditoluene-*p*-sulphonamidonaphthalene. Owing to the minute yield and the fact that repetition often failed to produce anything but tar the method was abandoned. Other methods of acylating this diamine proved equally ineffective and attention was turned to alternative syntheses. A likely route to (III), *viz.*, from 4-bromo-8-nitro-1-naphthylamine by toluenesulphonation, reduction, and further action of toluene-*p*-sulphonyl chloride could not be achieved as the amine failed to react with toluene-*p*-sulphonyl chloride.

Finally the following method was adopted. 8-Nitro-1-toluene-*p*-sulphonamidonaphthalene (IV) underwent smooth bromination in glacial acetic acid, and the orientation of the bromine atom in the product (V) was proved by hydrolysis to 4-bromo-8-nitro-1-naphthylamine (Hodgson and Crook, *J.*, 1936, 1338). (V) on reduction gave (VI), and the latter was readily converted into 4-bromo-1 : 8-ditoluene-*p*-sulphonamidonaphthalene, identical with the bromination product of 1 : 8-ditoluene-*p*-sulphonamidonaphthalene.



(IV.) (V.) (VI.)

(Ts = *p*-$C_6H_4Me{\cdot}SO_2$)

Consden and Kenyon (*J.*, 1935, 1591) have shown that bromine reacts with 1-toluene-*p*-sulphonamidonaphthalene in chloroform, yielding 4-bromo-1-toluene-*p*-sulphonamidonaphthalene. As the toluenesulphonamido-groups in 1 : 8-ditoluene-*p*-sulphonamidonaphthalene are reinforcing each other as regards electrophilic substitution in the naphthalene nucleus, it might have been expected that under similar conditions dibromination would have occurred. The experimentally observed monbromination can thus be considered abnormal and perhaps savours of steric hindrance. Also, the bromination of 1 : 5- and 1 : 8-ditoluene-*p*-sulphonamidonaphthalenes in pyridine, which might have yielded polybromo-derivatives (cf. Consden and Kenyon, *loc. cit.*; Bell, *J.*, 1932, 2732), proved to be a complex reaction from which no pure products were isolated.

The nitration of 4-bromo-1 : 8-ditoluene-*p*-sulphonamidonaphthalene in glacial acetic acid proceeded normally, the product being 4-bromo-2 : 5 : 7-trinitro-1 : 8-ditoluene-*p*-sulphonamidonaphthalene. The latter underwent quantitative hydrolysis with concentrated sulphuric acid, yielding the corresponding diamine.

Experimental.

(All m. p.s are uncorrected.)

Bromination of 1 : 5-*Ditoluene*-p-*sulphonamidonaphthalene.*—The compound (10 g.), suspended in glacial acetic acid (300 c.c.), was treated with bromine (4 c.c.) in glacial acetic acid (20 c.c.) at 95° whilst being stirred. After 10 minutes the solution was cooled and the silvery needles collected (7·7 g.). Recrystallisation from nitrobenzene afforded colourless needles of 4 : 8-*dibromo*-1 : 5-*ditoluene*-p-*sulphonamidonaphthalene* (6·8 g.), m. p. 248° (decomp.) (Found: C, 46·3; H, 3·3; N, 4·8; Br, 24·9. $C_{24}H_{20}O_4N_2S_2Br_2$ requires C, 46·2; H, 3·2; N, 4·5; Br, 25·6%). The compound is readily soluble in aqueous alkalis, moderately soluble in pyridine, but sparingly soluble in the majority of organic solvents. A solution of the sulphonamide (5 g.) in sulphuric acid (50 c.c.; *d* 1·84) was kept for 24 hours and then poured on ice and water (*ca.* 300 g.). The pinkish-red solution was filtered and neutralised with aqueous ammonia at 0° (a temperature rise at this stage gives an uncrystallisable blue precipitate). The almost colourless precipitate was collected and dissolved in the minimum quantity of warm ethanol (charcoal; <60°), and the solution filtered. Cautious addition of water to the filtrate precipitated 4 : 8-*dibromo*-1 : 5-*naphthylenediamine* (0·4 g.) as long slender needles, decomposing explosively at 115° (Found: C, 37·0; H, 3·0; Br, 49·2. $C_{10}H_8N_2Br_2$ requires C, 38·0; H, 2·55; Br, 50·6%). The compound becomes blue, then purple, and finally black on storage, even in the dark. The addition of acetic anhydride (1 c.c.) to a solution of the amine (0·2 g.) in glacial acetic acid (1 c.c.) precipitated the *diacetyl* derivative (0·12 g.) which crystallised from warm nitrobenzene in colourless needles, darkening at 250° (Found: C, 42·8; H, 3·1; Br, 38·8. $C_{14}H_{12}O_2N_2Br_2$ requires C, 42·0; H, 3·0; Br, 40·0%).

Tetrazotisation and Coupling Reactions.—**4** : 8-Dibromo-1 : 5-ditoluene-*p*-sulphonamidonaphthalene (10 g.) was stirred into sulphuric acid (60 c.c.; *d* 1·84) and after 36 hours the solution was poured on ice and water (300 g.) and filtered. Sodium nitrite (4 g.) in water (40 c.c.) was added at 0°, and after 5 minutes sufficient urea to destroy the excess of nitrous acid. The solution was then divided into four equal parts and the portions added severally at 0° to solutions of (*a*) cuprous chloride (10 g.) in hydrochloric acid (150 c.c.; *d* 1·18), (*b*) cuprous bromide (10 g.) in hydrobromic acid (150 c.c.; *d* 1·7), (*c*) potassium iodide (10 g.) in water (100 c.c.), and (*d*) 2-naphthol (5 g.) in 20% sodium hydroxide solution (200 c.c.). The products isolated were (*a*) **4** : 8-*dibromo*-1 : 5-*dichloronaphthalene* (0·65 g.) which after recrystallisation from aqueous acetic acid (charcoal) was obtained in colourless needles, m. p. 142° (Found : C, 34·6; H, 1·1; Halogen, 62·1. $C_{10}H_4Cl_2Br_2$ requires C, 33·8; H, 1·1; Halogen, 65·0%), (*b*) 1 : 4 : 5 : 8-*tetrabromonaphthalene* (0·67 g.), which separated from glacial acetic acid (charcoal) in colourless needles and prisms, m. p. 145° (Found : C, 27·8; H, 1·0; Br, 70·9. $C_{10}H_4Br_4$ requires C, 27·1; H, 0·9; Br, 72·0%), (*c*) 1 : 5-*dibromo*-**4** : 8-*di-iodonaphthalene* (1·35 g.), which crystallised from glacial acetic acid (charcoal) in silvery plates, m. p. 148° (Found : C, 22·7; H, 0·8; Halogen, 74·8. $C_{10}H_4Br_2I_2$ requires C, 22·3; H, 0·75; Halogen, 76·9%), and (*d*) **4** : 8-*dibromo*-1 : 5-*naphthylene-bisazo*-2-*naphthol* (2·4 g.), which formed scarlet needles, m. p. 272° (decomp.), from nitrobenzene, and which imparted a beautiful blue colour to concentrated sulphuric acid (Found : N, 9·2. $C_{30}H_{18}O_2N_4Br_2$ requires N, 8·95%).

Deamination of **4** : 8-*Dibromo*-1 : 5-*naphthylenediamine.*—The sulphonamide (5 g.) was stirred into sulphuric acid (50 c.c.; *d* 1·84) and after 36 hours a solution of sodium nitrite (2 g.) in sulphuric acid (25 c.c.; *d* 1·84) was added. The solution was cooled to 0° and treated with glacial acetic acid (150 c.c.), after which it was added to vigorously stirred ethanol (300 c.c.; 100%) containing freshly prepared cuprous oxide (5 g.). When effervescence had ceased, the bulk of ethyl acetate and excess of ethanol were distilled off under reduced pressure, and water (*ca.* 500 c.c.) was added to the solution. After 24 hours, the solids were removed and extracted with boiling ethanol (charcoal), whereupon 1 : 5-dibromonaphthalene (0·35 g.) crystallised from the cold extract. After two recrystallisations from ethanol it had m. p. 130°, alone and mixed with an authentic specimen prepared from 1 : 5-naphthylenediamine (Found : C, 41·9; H, 2·4; Br, 54·3. Calc. for $C_{10}H_6Br_2$: C, 42·0; H, 2·1; Br, 55·9%).

Bromination of 1 : 5- *and* 1 : 8-*Dinitronaphthalenes.*—The directions given by Dhar (*loc. cit.*) were followed and the resulting compound was crystallised several times from benzene in each case. 1 : 5-Dinitronaphthalene (5 g.) yielded a tetrabromonaphthalene, m. p. 231° (0·95 g.); 1 : 8-dinitronaphthalene (5 g.) also yielded the same substance (0·37 g.) (Found : Br, 73·2. Calc. for $C_{10}H_4Br_4$: Br, 72·0%). Treatment of 1 : 5-dinitronaphthalene (5 g.) with bromine (2·5 c.c.) and a crystal of iodine at 220° for 18 hours also yielded the same compound (0·60 g.).

Bromination of 1 : 5-*Dibromonaphthalene.*—This compound was brominated in the absence of a solvent (cf. Zalkind and Belikov, *loc. cit.*) for comparison with the above. The compound (2 g.) was heated with bromine (2·4 g.) and a crystal of iodine in a sealed tube at 200° for 6 hours. The product was washed with warm water, dried, and crystallised repeatedly from benzene, yielding the same tetrabromonaphthalene, m. p. 231°, undepressed on admixture with either of the above specimens.

Nitration of **4** : 8-*Dibromo*-1 : 5-*ditoluene*-p-*sulphonamidonaphthalene.*—The substance (1 g.), suspended in glacial acetic acid (10 c.c.) containing sodium nitrite (0·05 g.), was treated in the cold with nitric acid (1·5 c.c.; *d* 1·52), and the mixture left overnight. The yellow residue (0·65 g.) was crystallised first from alcoholic pyridine and then from nitrobenzene. *4-Bromo-2 : 6 : 8-trinitro*-1 : 5-*ditoluene*-p-*sulphonamidonaphthalene* was obtained in yellow needles, m. p. 245° (decomp.) (Found : C, 42·8; H, 2·6; N, 10·3; Br, 12·9. $C_{24}H_{18}O_{10}N_6BrS_2$ requires C, 42·35; H, 2·7; N, 10·3; Br, 11·75%). Hydrolysis was accomplished when the compound (0·5 g.) in sulphuric acid (5 c.c.; *d* 1·84) after being at 40° for 2 hours was poured into water. The precipitated *4-bromo-2 : 6 : 8-trinitro*-1 : 5-*naphthylenediamine* (0·25 g., *ca.* 100%) when crystallised from nitrobenzene formed deep red needles with a purplish tinge, m. p. 258° (decomp.) (Found : C, 32·7; H, 1·6. $C_{10}H_4O_6N_6Br$ requires C, 32·3; H, 1·6%).

Bromination of 5-*Nitro*-1-*toluene*-p-*sulphonamidonaphthalene.*—The compound (1 g.), made according to the directions of Hodgson and Turner (*loc. cit.*), was treated in glacial acetic acid (30 c.c.) at 95° with a 10% (v/v) solution of bromine in the same solvent (3·5 c.c.). After 2 hours at this temperature the mixture was left overnight. The addition of water to this solution precipitated a colourless mixture of monobromo-compounds (0·77 g.), which was crystallised six times from aqueous acetic acid. *4-Bromo-5-nitro*-1-*toluene*-p-*sulphonamidonaphthalene* was obtained in colourless needles (0·12 g.), m. p. 204° (Found : C, 48·7; H, 3·1; Br, 17·5. $C_{17}H_{13}O_4N_2BrS$ requires C, 48·5; H, 3·1; Br, 19·0%). Hydrolysis of the substance (0·10 g.) with sulphuric acid (3 c.c.; *d* 1·84) at 45° for 2 hours, and subsequent addition of ice (50 g.) followed by ammonia, gave the *amine* which crystallised from ethanol in orange needles (0·02 g.), m. p. 129·5° (Found : C, 45·2; H, 2·7. $C_{10}H_7O_2N_2Br$ requires C, 45·0; H, 2·6%). It gave a large depression of melting point when mixed with an authentic specimen of 2-bromo-5-nitro-1-naphthylamine prepared by the bromination of 5-nitro-1-naphthylamine, according to Hodgson and Turner (*loc. cit.*).

Bromination of 1 : 8-*Ditoluene*-p-*sulphonamidonaphthalene.*—(a) *In chloroform.* The substance (10 g.) in chloroform (200 c.c.) was treated with a solution of bromine (2·3 c.c.) in the same solvent (20 c.c.) at *ca.* 60°. The solution evolved much hydrogen bromide, and it was evaporated almost to dryness. Crystallisation of the residue (8·8 g.), first from toluene (charcoal) and then from glacial acetic acid, gave *4-bromo*-1 : 8-*ditoluene*-p-*sulphonamidonaphthalene* as colourless fine needles (6·7 g.), m. p. 208° (Found : C, 52·9; H, 3·8; N, 5·0; Br, 15·2; S, 11·5. $C_{24}H_{21}O_4N_2BrS_2$ requires C, 52·8; H, 3·9; N, 5·1; Br, 14·65; S, 11·75%).

(b) *In glacial acetic acid.* The compound (2 g.), dissolved in the minimum quantity of glacial acetic acid (*ca.* 12 c.c.), was treated at *ca.* 80° with a solution of bromine in glacial acetic acid (6·5 c.c.; 10% v/v)

with stirring. The crystalline precipitate (1·2 g.) obtained on cooling was recrystallised from glacial acetic acid; 4-bromo-1 : 8-ditoluene-*p*-sulphonamidonaphthalene separated in long colourless needles (0·72 g.), m. p. 208°, alone and mixed with the previous specimen (Found : Br, 15·0%). It was soluble in the usual solvents. A solution of the compound (1 g.) in sulphuric acid (20 c.c.; *d* 1·84) was kept for 4 days at 20° and then poured on ice; the solution was filtered, rendered alkaline with aqueous ammonia, and extracted with ether, giving a pale yellowish-green solution in the latter, which after being dried and then saturated with dry hydrogen chloride furnished a minute amount of a colourless to grey *hydrochloride* (Found : Halogen, 45·5. $C_{10}H_{10}N_2ClBr$ requires Halogen, 42·2%). The free base, liberated with dilute aqueous ammonia, proved highly unstable.

4-*Bromo*-2 : 5 : 7-*trinitro*-1 : 8-*ditoluene*-p-*sulphonamidonaphthalene* was obtained when 4-bromo-1 : 8-ditoluene-*p*-sulphonamidonaphthalene (1 g.) in glacial acetic acid (5 c.c.) containing sodium nitrite (0·05 g.) was treated cautiously with nitric acid (0·5 c.c.; *d* 1·52) in glacial acetic acid (0·5 c.c.) below 60°. After 3 hours at 0°, the precipitated *compound* (0·65 g.) was collected, dried, and crystallised from glacial acetic acid. It formed clusters of yellow prisms and rhombs, m. p. 204° (decomp.) (Found : C, 43·1; H, 2·7; N, 10·6; Br, 11·6. $C_{24}H_{15}O_{10}N_5BrS_2$ requires C, 42·35; H, 2·7; N, 10·3; Br, 11·75%). When the substance in sulphuric acid [0·3 g. in 5 c.c. (*d* 1·84)] was kept at 40° for 1 hour and then poured into water, 4-*bromo*-2 : 5 : 7-*trinitro*-1 : 8-*naphthylenediamine* separated, and crystallisation from nitrobenzene gave needles, m. p. 268° (decomp.) (Found : C, 32·0; H, 1·9. $C_{10}H_4O_6N_5Br$ requires C, 32·3; H, 1·6%). On being crystallised from acetone it gave brown-red pyramids of 6-*bromo*-1 : 2-*dihydro*-2 : 2′-*dimethyl*-4 : 7 : 9-*trinitroperimidine*, m. p. 264° (Found : N, 17·4. $C_{13}H_{10}O_6N_5Br$ requires N, 17·0%).

1-*Bromo*-4 : 5-*dinitronaphthalene*.—The method of Hodgson and Hathway was replaced by a modification of that of Merz and Weith (*loc. cit.*). The 1-bromonaphthalene required was made by a method similar to that reported in *Org. Synth.* (Coll. Vol. I, 2nd edn., p. 121), but less bromine was used as it was found that naphthalene was a more tolerable impurity in the product than dibromonaphthalenes.

A solution of bromine (80 c.c.) in chloroform (200 c.c.) was led beneath the surface of a rapidly stirred solution of naphthalene (200 g.) in chloroform (300 c.c.) at *ca.* 40°. Hydrogen bromide was copiously evolved and after 24 hours at room temperature the bulk of the solvent was removed at reduced pressure. Finely powdered potassium hydroxide was then added to the resulting oil which thereupon assumed a clear yellow colour. After 6 hours at 50°, the oil was filtered and distilled in a current of air. At 150° some hydrogen bromide was evolved and the first runnings (at 230—240°) solidified to naphthalene. The second fraction (220 g.) was collected at 265—280° and redistilled. 1-Bromonaphthalene (190 g.) was obtained as a pale yellow oil, b. p. 272—273°/740 mm.

The substance (50 g.) was added dropwise to nitric acid [150 c.c. (*d* 1·52) + 75 c.c. (*d* 1·42)] at *ca.* 0—5°, and the mixture was then heated cautiously at *ca.* 80° for 30 minutes. After the mixture had been cooled to 0°, ice (*ca.* 500 g.) was added and the mixture was heated on the water-bath until no more brown fumes were evolved. The solid residue was crystallised three times from aqueous acetic acid; 1-bromo-4 : 5-dinitronaphthalene was thus obtained as long very pale yellow needles (15·4 g.), m. p. 168°, alone or mixed with a specimen prepared by the method of Hodgson and Hathway (*loc. cit.*) (Found : N, 9·7. Calc. for $C_{10}H_4O_4N_2Br$: N, 9·4%).

Reduction of 1-*Bromo*-4 : 5-*dinitronaphthalene*.—The compound (5 g.) in glacial acetic acid (150 c.c.) at 90° was treated with stannous chloride (25 g.) in glacial acetic acid (150 c.c.) previously saturated with dry hydrogen chloride. On cooling, the pale yellow needles of the bromodiamine *stannichloride* (4·7 g.) were collected (if crystallisation is delayed it is started by passing dry hydrogen chloride through the solution) (Found : N, 6·3; Halogen, 45·9; Sn, 13·7. $2C_{10}H_5N_3Br,H_2SnCl_6$ requires N, 6·9; Halogen, 46·1; Sn, 14·7%). The diamine liberated from the stannichloride with aqueous sodium carbonate (decomposition was slow and sodium hydroxide gave an inferior product) was extracted with ether, and from this solution the *monohydrochloride* (Found : Cl, 12·5. $C_{10}H_5N_3Br,HCl$ requires Cl, 13·0%) and the *sulphate* (Found : SO_4, 16·6. $2C_{10}H_5N_3Br,H_2SO_4$ requires SO_4, 16·8%) were made by adding ether containing hydrogen chloride and sulphuric acid respectively.

Bromination of 8-*Nitro*-1-*toluene*-p-*sulphonamidonaphthalene*.—The substance (4 g.) in glacial acetic acid (40 c.c.) was treated with a solution of bromine in glacial acetic acid (6·4 c.c.; 10% v/v) at 50° and, after cooling, the crystalline deposit (2·75 g.) was removed and recrystallised from glacial acetic acid (charcoal). 4-*Bromo*-8-*nitro*-1-*toluene*-p-*sulphonamidonaphthalene* separated therefrom in long colourless needles (2·01 g.), m. p. 225° (Found : C, 49·1; H, 3·5; Br, 18·9. $C_{17}H_{11}O_4N_2BrS$ requires C, 48·5; H, 3·1; Br, 19·0%). A solution of the compound (0·2 g.) in sulphuric acid (5 c.c.; *d* 1·84) was kept at 50° for 30 minutes and then poured on ice and water (50 g.). The precipitated crystalline amine sulphate was collected and treated with an excess of aqueous ammonia, and the residue crystallised from aqueous acetic acid. 4-Bromo-8-nitro-1-naphthylamine separated in fawn-red needles (0·06 g.), m. p. 115°, undepressed by a specimen obtained by the method of Hodgson and Crook (*loc. cit.*) (Found : N, 10·2. Calc. for $C_{10}H_7O_2N_2Br$: N, 10·5%).

1-*Amino*-5-*bromo*-8-*toluene*-p-*sulphonamidonaphthalene*.—4-Bromo-8-nitro-1-toluene-*p*-sulphonamidonaphthalene (1 g.) in glacial acetic acid (15 c.c.) was treated with a solution of stannous chloride (3 g.) in glacial acetic acid–dry hydrogen chloride (15 c.c.), and the solution was then evaporated almost to dryness on the water-bath at reduced pressure. The crystalline residue was then treated with aqueous sodium carbonate, and the solids were removed and extracted with hot ethanol, from which, after evaporation at reduced pressure and cautious addition of water, 1-*amino*-5-*bromo*-8-*toluene*-p-*sulphonamidonaphthalene* separated in colourless needles (0·24 g.), m. p. 193° (decomp.) (Found : C, 52·2; H, 4·2. $C_{17}H_{13}O_2N_2BrS$ requires C, 52·2; H, 3·9%). It appeared to be sparingly soluble in dilute sodium hydroxide solution, but was soluble in the usual organic solvents.

4-*Bromo*-1 : 8-*ditoluene*-p-*sulphonamidonaphthalene*.—The preceding compound (0·2 g.), toluene-*p*-sulphonyl chloride (0·1 g.), and pyridine (3 c.c.) were heated together at 95° for 30 minutes, and, after the mixture had cooled, dilute sulphuric acid was added. The solid was collected, washed, dried, and crystallised three times from chloroform. 4-Bromo-1 : 8-ditoluene-*p*-sulphonamidonaphthalene was obtained as fine felted needles (0·07 g.), m. p. 208°, undepressed on admixture with the bromination product of 1 : 8-ditoluene-*p*-sulphonamidonaphthalene.

The author gladly acknowledges Dr. H. H. Hodgson's permission further to develop investigations carried out with him at Huddersfield during 1943—44 and thanks him for his interest in this work. The author also thanks Professor D. H. Hey for permission to use an autoclave at King's College, London, and acknowledges financial aid from the Council of the University College, Exeter, and Imperial Chemical Industries Limited.

WASHINGTON SINGER LABORATORIES, PRINCE OF WALES ROAD,
UNIVERSITY COLLEGE OF THE SOUTH WEST, EXETER. [*Received, July 14th*, 1950.]

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47. *Substitution Reactions of the Naphthylenediamines. Part III. The Bromination of* 1 : 5- *and* 1 : 8-*Naphthylenediamines and Related Compounds.*

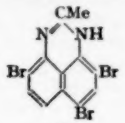
By J. S. WHITEHURST.

Bromination of 1 : 8-naphthylenediamine in glacial acetic acid gave first 2 : 4 : 7-tribromo-1 : 8-naphthylenediamine and then 4 : 7 : 9(or 4 : 6 : 9)-tribromo-2-methylperimidine dibromide. 2-Methylperimidine on bromination yielded a monobromo-2-methylperimidine, a dibromo-compound, and a dibromide of the latter, and on nitration a dinitro-compound. Although 1 : 5-naphthylenediamine and bromine produced substances of high molecular weight, the diacetyl derivative readily gave 1 : 5-diacetamido-4 : 8-dibromonaphthalene. 1 : 8-Dibenzamidonaphthalene, under similar conditions, lost a benzoyl group and was converted into a brominated 2-phenylperimidine, identical with the bromination product of 2-phenylperimidine itself.

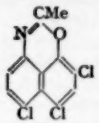
1 : 8-NAPHTHYLENEDIAMINE, on treatment with excess of bromine in hot glacial acetic acid solution, gave, in high yield, a tribromo-2-methylperimidine dibromide, the *peri*-diamine groups having been involved in ring closure with one molecule of acetic acid. It was thought desirable to establish, not only the constitution of this substance, but also the approximate course of the reaction—whether, for instance, ring closure had occurred before or after the introduction of any of the bromine atoms. It was found that 1 : 8-naphthylenediamine was not substantially converted into 2-methylperimidine by hot glacial acetic acid, and that 2-methylperimidine, brominated under conditions similar to those employed for the diamine, gave a dibromo-2-methylperimidine dibromide. Furthermore, by use of only three molecular proportions of bromine in glacial acetic acid, 1 : 8-naphthylenediamine yielded a tribromo-diamine. Clearly, ring closure occurs after the entry of all three bromine atoms.

Tetrazotisation of the tribromo-diamine proved difficult, and the tribromonaphthalene obtained by deamination with ethanol was accompanied by a *peri*-triazine derivative. The melting point of the former was gradually raised to 95—96°. Attempts to increase the yield by deamination with hypophosphorous acid were unsuccessful. Obviously, unless anomalous *meta*-substitution has occurred, the bromine atoms in the tribromo-1 : 8-naphthylenediamine must be in either the 2 : 4 : 5- or the 2 : 4 : 7-positions, and therefore this tribromonaphthalene is either the 1 : 3 : 8- or the 1 : 3 : 6-compound. The former is yet unknown, but the latter was prepared by Claus and Jäck (*J. pr. Chem.*, 1898, **57**, 18) from 1 : 3 : 6-tribromo-2-naphthylamine, the constitution of which was established by Franzen and Stauble (*ibid.*, 1920, **101**, 59) [cf. Fries and Schimmelschmidt, *Annalen*, 1930, **484**, 248 (Note 1), 250 (Note 1)]. 1 : 3 : 6-Tribromo-2-naphthylamine has been obtained from 1-bromo-2-naphthylamine, by bromination in chloroform (Claus and Philipson, *J. pr. Chem.*, 1891, **43**, 56); from 2-toluene-*p*-sulphonamidonaphthalene, by bromination first in chloroform (which produces the 1 : 6-derivative) and then in pyridine, followed by hydrolysis (Bell, *J.*, 1932, 2732); and from benzylidene-2-naphthylamine, by repeated bromination and rearrangement of the products (Franzen and Aaslund, *J. pr. Chem.*, 1917, **95**, 160). Of these methods, that of Bell appeared the most promising. This author gives few experimental details for the preparation of 1 : 6-dibromo-2-toluene-*p*-sulphonamidonaphthalene and under the conditions employed by us it was found that the major product was

1 : 6-dibromo-2-naphthylamine hydrobromide, obviously formed by hydrolysis of the initially formed sulphonamide. Also, contrary to the statement of Claus and Philipson (*loc. cit.*), the bromination of 1-bromo-2-naphthylamine in chloroform did not proceed further than the formation of the same dibromonaphthylamine hydrobromide. However, 1 : 6-dibromo-2-naphthylamine on being rapidly treated with excess of bromine in hot chloroform produced 1 : 3 : 6-tribromo-2-naphthylamine hydrobromide, the formation of this compound being noteworthy in that Claus *et al.* (*loc. cit.*) failed to detect any basic properties of the amine. Diazotisation in sulphuric acid–glacial acetic acid, followed by deamination with ethanol, afforded, in good yield, 1 : 3 : 6-tribromonaphthalene, m. p. 100—101°, undepressed on admixture with the substance, m. p. 95—96°, prepared earlier. Microscopical examination of the two specimens under polarised light revealed their identity. Hence it was concluded that 1 : 8-naphthylenediamine had undergone bromination to yield 2 : 4 : 7-tribromo-1 : 8-naphthylenediamine and 4 : 7 : 9(or 4 : 6 : 9)-tribromo-2-methylperimidine (I). The two structures which can be written for the latter are probably identical, as this is almost certainly a case of hydrogen-bond mesomerism (cf. Hunter, *J.*, 1945, 806, for similar cases).



(I.)



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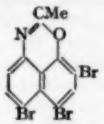

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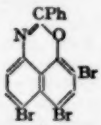

(IV.)

These results may be compared with those of Fichter *et al.* (*Ber.*, 1906, **39**, 3331; 1909, **42**, 4748) on the halogenation of 8-acetamido-1-naphthol and 8-benzamido-1-naphthol. Chlorination of the former in acetone yielded (II), and bromination in glacial acetic acid was reported to give the dibromide of (III). Under similar conditions, 8-benzamido-1-naphthol and bromine produced (IV). However, in none of these compounds was the orientation of the halogen atoms proved, and it was unfortunate that the halogenation of 8-amino-1-naphthol itself in glacial acetic acid was not reported.

When less bromine was used, 2-methylperimidine yielded a monobromo-compound, m. p. 181°, and a dibromo-compound, m. p. 217—219° (decomp.), and, as electrophilic substitution would be expected to occur in the naphthalene nucleus *ortho* and *para* to the nitrogen atoms, the former is either 4(9)- or 6(7)-bromo-2-methylperimidine. Hodgson and Hathway (*J.*, 1945, 543) have described 6(7)-bromo-2-methylperimidine (m. p. 131°), but attempts to repeat their work proved abortive. The possible nuclear-substituted dibromo-2-methylperimidines would seem to be the 4 : 6-, 7 : 9-, 4 : 7-, 6 : 9-, 6 : 7-, and 4 : 9-compounds, but of these the 4 : 6- and 7 : 9-structures are probably resonance forms of the same substance, and similar considerations apply to the 4 : 7- and 6 : 9-compounds. At any rate, the separate existence of tautomers in these pairs would be unrealisable under ordinary conditions. Hodgson and Crook (*J.*, 1936, 1338) have described 7 : 9-dibromo-2-methylperimidine, and this work was amply confirmed as far as the preparation of the stannichloride of the desired product, but the liberation of the latter proved extraordinarily difficult and the green solution obtained in the presence of ether or benzene furnished a dark green substance, m. p. *ca.* 150—160°. In these circumstances no conclusions could be drawn concerning the structures of these brominated 2-methylperimidines. On the other hand, after 1 : 8-naphthylenediamine had been treated in benzene with acetyl chloride, bromination of the basified product in acetic acid furnished 4 : 6(7) : 9-tribromo-2-methylperimidine, identical with a specimen made from 2 : 4 : 7-tribromo-1 : 8-naphthylenediamine and acetic anhydride. As 2-methylperimidine has been found to undergo bromination only so far as a dibromo-compound this must mean that the reaction product of 1 : 8-naphthylenediamine and acetyl chloride must contain either 8-acetamido-1-naphthylamine or unchanged 1 : 8-naphthylenediamine. None of the latter was detected.

The nitration of 2-methylperimidine in glacial acetic acid was parallel to that of bromination. After the initial separation of 2-methylperimidine nitrate, a dinitro-compound was formed. 1 : 5-Diacetamidonaphthalene, on nitration either in glacial acetic acid or in fuming nitric acid, gave yellow amorphous substances which proved intractable, but on bromination it gave a dibromo-derivative apparently identical with 1 : 5-diacetamido-4 : 8-dibromonaphthalene. Hence the bromination of 1 : 5-diacetamidonaphthalene occurs in the same sense as that of 1 : 5-ditoluene-*p*-sulphonamidonaphthalene (cf. Part II, preceding paper). Many fruitless attempts were made to prepare 1 : 8-diacetamidonaphthalene. Reaction of the diamine with

acetic anhydride in aqueous alcoholic potassium hydroxide gave a blue solution containing unchanged diamine. In other media the only isolable product was 2-methylperimidine. 1 : 8-Dibenzamidonaphthalene, on bromination in glacial acetic acid, was converted into a compound $C_{17}H_8N_2Br_6$, which is clearly a brominated 2-phenylperimidine. During this reaction, one benzoyl group has been hydrolysed and the other has undergone ring closure. 2-Phenylperimidine, brominated under similar conditions, gave the same compound. Its structure has not yet been settled.

The bromination of 1 : 5-naphthylenediamine took place in an entirely unexpected manner, and was studied in a variety of media including water, dilute hydrochloric acid, benzene, ethanol, chloroform, carbon tetrachloride, ethylene dichloride, glacial acetic acid, and pyridine. In the last two solvents, the addition of bromine immediately gave amorphous black precipitates; in other media, in particular chloroform and carbon tetrachloride, the products were indigo-coloured. Dilute sodium carbonate solution removed practically no hydrobromic acid from these precipitates, and as they were virtually insoluble in organic solvents, and decomposed gradually when heated to high temperatures, they must have contained compounds of high molecular weight. Analysis of two products, (A) and (B) (see Experimental Section), the former obtained by employing 0·1 mole of bromine in chloroform, the latter by using excess of bromine in glacial acetic acid, showed clearly that the maximum amount of bromine introduced into the naphthalene molecule corresponded to one atom. The difference in the behaviour of 1 : 5- and 1 : 8-naphthylenediamines towards bromine is probably due to 1 : 5-naphthaquinone structures being possible whereas 1 : 8-naphthaquinone structures are not (Vesely and Jakes, *Bull. Soc. chim.*, 1923, **33**, 955). Most likely 1 : 5-naphthylenediamine is converted initially into a monobromonaphthylenediamine, the bromine atom perhaps entering position 2 (cf. the bromination of 1 : 5-dihydroxynaphthalene; Wheeler and Ergle, *J. Amer. Chem. Soc.*, 1930, **52**, 4872; Carter, Race, and Rowe, *J.*, 1942, 236); this may be oxidised to a highly reactive 1 : 5-naphthaquinonedi-imine which combines with excess of naphthylenediamine to produce (A). Further action of bromine will give rise to (B). The formation of these substances may be analogous to that of the highly coloured substances obtained by Thompson (*J. Org. Chem.*, 1948, **13**, 371) from 1 : 5-dihydroxynaphthalene and chlorine in glacial acetic acid solution.

Another possible synthesis of halogeno-diamines, *viz.*, from mercuri-compounds, proved impracticable as both diamines reduced mercuric acetate to the mercurous salt. The latter was precipitated almost immediately on mixing of glacial acetic solutions of mercuric acetate and 1 : 5-naphthylenediamine. The fate of the latter was not investigated in detail, although it was found that an equivalent molar quantity of 1 : 5-dihydroxynaphthalene yielded the same amount of mercurous acetate. As 1 : 5-dihydroxynaphthalene is known to be oxidised to juglone (Bernsthen and Semper, *Ber.*, 1887, **20**, 939) it seems that this compound is also produced from the diamine. Although 1 : 8-naphthylenediamine was also oxidised by mercuric acetate in glacial acetic acid no separation of mercurous acetate occurred until ethanol was added to the solution. It seems probable, therefore, that the oxidation of this diamine takes a different course from that of the 1 : 5-isomer, a fact observed by Willstätter and Wheeler (*Ber.*, 1914, **47**, 2798) in contrast to the claim of Erdmann (*Annalen*, 1888, **247**, 358) in the case of the corresponding dihydroxynaphthalenes.

Experimental.

(M. p.s are uncorrected.)

Bromination of 1 : 5-*Naphthylenediamine.*—(*a*) *In chloroform.* The diamine (1 g.) in chloroform (150 c.c.) was treated with a 1% (v/v) solution of bromine in chloroform (3 c.c.) with vigorous stirring at 15°. The indigo-coloured precipitate was washed with chloroform (50 c.c. in all), dried, and extracted with warm (40°) 2% sodium carbonate solution (100 c.c.) and dried again (product A). (*b*) *In glacial acetic acid.* The diamine (1 g.) in glacial acetic acid (50 c.c.) was treated with a solution of bromine (1·2 c.c.) in glacial acetic acid (10 c.c.) with vigorous stirring at 15°. The almost black precipitate was washed with glacial acetic acid (20 c.c.), dried, extracted with sodium carbonate solution (100 c.c.) as above, and dried again (product B). Both products shrank at *ca.* 250°, but did not melt at 350°, and were insoluble in the usual solvents [Found (first values for A, second for B): C, 62·4, 49·6; H, 4·6, 3·1; N, 14·7, 11·6; Br, 16·6, 33·8. Calc. for $C_{10}H_5Br{\cdot}(NH_2)$: C, 50·65; H, 3·8; N, 11·8; Br, 33·7. Calc. for $C_{10}H_4(NH_2)_2$: C, 75·9; H, 6·4; N, 17·7; Br, 0·0%].

Bromination of 1 : 5-*Diacetamidonaphthalene.*—The compound (1 g.) in glacial acetic acid (50 c.c.) was treated with a solution of bromine (0·8 c.c.) in glacial acetic acid (5 c.c.) at *ca.* 90° with stirring. The initially formed oil rapidly solidified and on crystallisation from hot nitrobenzene gave colourless needles of 1 : 5-diacetamido-4 : 8-dibromonaphthalene (0·7 g.) (Found: C, 42·7; H, 3·1; Br, 37·8. Calc. for $C_{14}H_{12}O_2N_2Br_2$: C, 42·0; H, 3·0; Br, 40·0%). The compound darkened at *ca.* 250° and decomposed continuously above this temperature without forming a sublimate.

Bromination of 1 : 8-*Dibenzamidonaphthalene.*—A solution of bromine in glacial acetic acid (2·5 c.c.; 10% v/v) was added to the compound (0·32 g.) in glacial acetic acid (100 c.c.) at 90°. On cooling, beautiful orange-coloured needles crystallised from the solution (0·29 g.). The *substance* was sparingly soluble in the usual solvents. It darkened at 200° and melted at 235—240° (decomp.) (Found : C, 28·7; H, 1·23; N, 3·7; Br, 66·7. $C_{17}H_8N_2Br_6$ requires C, 28·4; H, 1·1; N, 3·9; Br, 66·6%).

2-*Phenylperimidine.*—This compound was made according to the directions of Sachs (*Annalen*, 1909, **365**, 94), as well as by the following method : 1 : 8-Naphthylenediamine (1 g.) in boiling benzene (25 c.c.) was treated with benzoic anhydride (2 g.). After 2 hours the benzene was slowly distilled off and the resulting gum left with 10% sodium hydroxide solution for a further 2 hours at *ca.* 50°. The crystalline residue was collected and recrystallised from aqueous ethanol (charcoal). 2-Phenylperimidine formed orange yellow needles (0·8 g.; m. p. 187—188°).

Bromination of 2-*Phenylperimidine.*—The compound (0·35 g.) in glacial acetic acid (100 c.c.) was treated with a solution of bromine in glacial acetic acid (5·5 c.c.; 10% v/v) at 90—95°. The mustard-yellow precipitate (0·80 g.) was collected, washed with a little glacial acetic acid, and dried in a vacuum (Found : C, 28·9; H, 1·3; N, 3·6; Br, 64·6%). No depression of melting point, 235—240° (decomp.), was observed when it was mixed with the previous specimen.

2-*Methylperimidine.*—The compound was best made by treating 1 : 8-naphthylenediamine (2 g.) with acetic anhydride (20 c.c.). Much heat was evolved; the diamine dissolved and the solution rapidly set to a mass of yellow needles of 2-methylperimidine acetate (2·0 g.). When crystallised from acetic anhydride it had m. p. 144° (Found : C, 69·1; H, 5·9. Calc. for $C_{14}H_{14}O_2N_2$: C, 69·4; H, 5·8%) (Sachs, *loc. cit.*, gives m. p. 130—140°). It was very soluble in the usual organic solvents, but sparingly soluble in cold acetic anhydride. Addition of aqueous ammonia to the aqueous solution liberated 2-methylperimidine, which crystallised from ethanol in pale greenish-yellow needles, m. p. 215—216° (decomp.) (Found : N, 15·2. Calc. for $C_{13}H_{10}N_2$: N, 15·4%).

Nitration of 2-*Methylperimidine.*—The compound (1 g.) in glacial acetic acid (10 c.c.) was treated dropwise with nitric acid (2 c.c.; *d* 1·42). The initial precipitate of 2-methylperimidine nitrate gradually dissolved and the reaction was completed by gentle warming on the water-bath. After filtration, the solution was treated with ethanol, and the orange-brown precipitate (m. p. *ca.* 180—190°) collected and crystallised from aqueous acetic acid. The *dinitro-2-methylperimidine* formed orange-yellow needles, darkening at 200° and melting at 238—240° to a deep-red liquid (Found : C, 53·2; H, 2·9; N, 20·2. $C_{13}H_8O_4N_4$ requires C, 52·9; H, 2·9; N, 20·6%). The nitration medium contained material which stained the fingers an intense orange-red.

Bromination of 2-*Methylperimidine.*—(a) *The monobromo-compound.* A vigorously stirred solution of the substance (0·3 g.) in glacial acetic acid (50 c.c.) was treated cautiously at 85—90° with a solution of bromine in glacial acetic acid (1·35 c.c., 1·5 moles; 10% v/v). On cooling, colourless nodules of the *hydrobromide* separated (0·19 g.), decomposing at *ca.* 300° (Found : Br′, 22·7. $C_{13}H_{10}N_2Br_2$ requires Br′, 23·4%), from which the *monobromo-2-methylperimidine* was liberated with aqueous ammonia. It crystallised from benzene in rosettes of pale green needles, m. p. 181° (Found : C, 55·1; H, 3·6; Br, 29·8. $C_{13}H_9N_2Br$ requires C, 55·2; H, 3·5; Br, 30·6%).

(b) *The dibromo-compound.* 2-Methylperimidine (0·4 g.) in well-stirred glacial acetic acid (90 c.c.) was treated with bromine in glacial acetic acid (3·6 c.c., 3 moles; 10% v/v) at 90°. The colourless *hydrobromide* (0·67 g.), m. p. 256—260° (decomp.) (Found : Br′, 18·4. $C_{13}H_9N_2Br_3$ requires Br′, 19·0%), which separated from the orange-coloured solution was collected and treated with aqueous ammonia, and the *dibromo-2-methylperimidine* was crystallised from benzene. It formed pale greenish-yellow needles which darkened at 200° and melted (decomp.) at 218—219° (Found : C, 42·7; H, 2·8; Br, 47·9. $C_{13}H_8N_2Br_2$ requires C, 42·4; H, 2·4; Br, 47·0%). The acetic acid filtrate from the above bromination on being poured into water produced a vivid blue colour.

(c) *The dibromo-compound dibromide.* A well stirred solution of 2-methylperimidine (0·5 g.) in glacial acetic acid (125 c.c.) was treated at 90—95° with a solution of bromine in the same solvent (6 c.c., 4·5 moles, 10% v/v). After cooling, the mustard-yellow needles [1·30 g.; m. p. *ca.* 225° (decomp.)] were collected, and a portion was crystallised from glacial acetic acid (in which it was sparingly soluble). The *dibromide* formed long mustard-yellow needles, m. p. 247° (decomp.) after darkening at 244° (Found : C, 28·1; H, 1·9; N, 5·2; Br, 62·6. $C_{13}H_8N_2Br_4$ requires C, 28·8; H, 1·6; N, 5·6; Br, 63·9%).

Bromination of 1 : 8-*Naphthylenediamine.*—(a) 2 : 4 : 7-*Tribromo*-1 : 8-*naphthylenediamine.* A vigorously stirred solution of 1 : 8-naphthylenediamine (0·5 g.) in glacial acetic acid (200 c.c.) at 90° was rapidly treated with a solution of bromine in the same solvent (5 c.c.; 10% v/v). On cooling, the shining silvery platelets of the *monohydrobromide* were removed, washed with a little glacial acetic acid, and dried in a vacuum (1·02 g.; darkens at 240° but is not molten at 320°) (Found : Br′, 16·2. $C_{10}H_8N_2Br_4$ requires Br′, 16·80%). It was decomposed with warm aqueous ammonia, and the liberated *tribromo-diamine*, recrystallised from ethanol, formed colourless rosettes of needles, m. p. 137—138° (Found : C, 30·7; H, 1·7; N, 6·9; Br, 60·2. $C_{10}H_7N_2Br_3$ requires C, 30·4; H, 1·8; N, 7·1; Br, 60·7%).

(b) *The dibromide of* 4 : 6(7) : 9-*tribromo-2-methylperimidine.* A solution of bromine (1 c.c.) in glacial acetic acid (5 c.c.) was added to a well stirred solution of 1 : 8-naphthylenediamine (0·5 g.) in glacial acetic acid (150 c.c.) at 95°. The yellow crystalline precipitate (1·5 g.) was collected, washed with a little glacial acetic acid, and dried in a vacuum. It is sparingly soluble in glacial acetic acid, crystallising therefrom in pale yellow needles, shrinking at *ca.* 250° and decomposing above this temperature (Found : C, 25·4; H, 1·6; Br, 68·2. $C_{13}H_7N_2Br_5$ requires C, 24·9; H, 1·2; Br, 69·0%).

4 : 6(7) : 9-*Tribromo-2-methylperimidine* was prepared from 2 : 4 : 7-tribromo-1 : 8-naphthylenediamine and boiling acetic anhydride. Addition of water to the cooled solution followed by crystallisation of the precipitate from benzene furnished yellow needles of the compound, m. p. 217—218°

(decomp.) after becoming green at *ca.* 200° (Found : C, 34·7; H, 1·8; N, 7·0; Br, 57·0. $C_{11}H_7N_2Br_3$ requires C, 34·4; H, 1·7; N, 6·7; Br, 57·2%). It was moderately soluble in ethanol, benzene, or glacial acetic acid.

4 : 6(7) : 9-*Tribromo-2-phenylperimidine* was formed from 2 : 4 : 7-tribromo-1 : 8-naphthylenediamine and benzoyl chloride in benzene solution. After being on a water-bath for 2 hours, the faint white precipitate was removed, and the solution concentrated in a vacuum. **4 : 6(7) : 9-Tribromo-2-phenylperimidine** separated from benzene in beautiful orange needles, darkening at 200° and melting (decomp.) at 215° (Found : C, 42·4; H, 1·9; Br, 50·1. $C_{17}H_9N_2Br_3$ requires C, 42·4; H, 1·9; Br, 49·9%). It was sparingly soluble in ethanol or glacial acetic acid.

1-Bromo-2-naphthylamine.—2-Acetonaphthalide (20 g.; m. p. 132°), prepared from 2-naphthylamine and acetic anhydride in benzene (Leonard and Boyd, *J. Org. Chem.*, 1946, **11**, 416; Ott and Levy, unpublished), was dissolved in the minimum amount of hot chloroform, and treated rapidly, with stirring, with a solution of bromine (12 c.c.) in chloroform (50 c.c.). The colourless precipitate of 1-bromo-2-acetonaphthalide hydrobromide [22 g.; m. p. 185—195° (decomp.)] (Franzen and Eidis, *J. pr. Chem.*, 1913, **88**, 760, give m. p. 180—190°) (Found : Br′, 22·7. Calc. for $C_{12}H_{11}ONBr_2$: Br′, 23·2%), was collected, dried, and decomposed with hot water. The resulting 1-bromo-2-acetonaphthalide, m. p. 138—139° (Lellmann and Schmidt, *Ber.*, 1887, **20**, 3154, and James and Judd, *J.*, 1914, 1433, give m. p. 140°), was added, in small portions, to boiling hydrochloric acid (500 c.c.; 15% w/v). After 15 minutes, the mixture was cooled and the crystalline 1-bromo-2-naphthylamine hydrochloride [9·5 g.; m. p. 225° (decomp.) after darkening at 200°] removed. Treatment with aqueous ammonia and crystallisation from aqueous ethanol yielded 1-bromo-2-naphthylamine, m. p. 63° (Franzen and Eidis, *loc. cit.*, give m. p. 63—64°) (Found : N, 6·0. Calc. for $C_{10}H_8NBr$: N, 6·3%).

1 : 3 : 6-*Tribromo-2-naphthylamine.*—1-Bromo-2-naphthylamine (2 g.) in hot chloroform (50 c.c.) was treated with bromine (1 c.c.) in chloroform (5 c.c.). The almost colourless precipitate of **1 : 6-*dibromo-2-naphthylamine hydrobromide*** [2·4 g.; m. p. 264° (decomp.)] (Found : Br′, 20·5. $C_{10}H_8NBr_3$ requires Br′, 20·9%) was treated with dilute aqueous sodium carbonate, and a portion of the residue was crystallised from ethanol. 1 : 6-Dibromo-2-naphthylamine separated therefrom in colourless needles, m. p. 119—120° (Franzen and Eidis, *loc. cit.*, give m. p. 122—123°). The remainder was dissolved in hot chloroform (50 c.c.) and bromine (1 c.c.) in chloroform (5 c.c.) added in one portion. The purple-red solution rapidly deposited orange needles of **1 : 3 : 6-*tribromo-2-naphthylamine hydrobromide*** [1·95 g.; m. p. 215—220° (decomp.)] (Found : Br′, 17·0. $C_{10}H_7NBr_4$ requires Br′, 17·35%), which after treatment with aqueous ammonia and crystallisation from ether (charcoal) furnished colourless very small needles of **1 : 3 : 6**-tribromo-2-naphthylamine, m. p. 143° (Claus and Philipson, *J. pr. Chem.*, 1891, **43**, 56, also give m. p. 143°) (Found : Br, 62·5. Calc. for $C_{10}H_8NBr_3$: Br, 63·1%).

1 : 3 : 6-*Tribromonaphthalene.*—The purple solution of **1 : 3 : 6**-tribromo-2-naphthylamine (0·5 g.) in sulphuric acid (8 c.c.; *d* 1·84) was treated with sodium nitrite (0·18 g.) dissolved in sulphuric acid (8 c.c.; *d* 1·84), and, at 0°, glacial acetic acid (25 c.c.) was added slowly. After 30 minutes the diazonium solution was poured into vigorously stirred absolute ethanol (150 c.c.) containing cuprous oxide (1 g.). After effervescence had ceased, the solution was decanted from precipitated inorganic matter, and evaporated on the water bath. Water (*ca.* 200 c.c.) was added and the colourless residue (0·4 g.; m. p. 90—95°) was crystallised twice from ethanol and once from ligroin. **1 : 3 : 6-Tribromonaphthalene** separated in colourless acicular crystals, m. p. 100—101° (Claus and Jäck, *loc. cit.*, give m. p. 98°) (Found : C, 32·6; H, 1·3; Br, 65·7. Calc. for $C_{10}H_5Br_3$: C, 32·9; H, 1·4; Br, 65·7%).

Deamination of **2 : 4 : 7-*Tribromo*-1 : 8-*naphthylenediamine.***—The diamine (0·5 g.) in sulphuric acid (15 c.c.; *d* 1·84) was treated with a solution of sodium nitrite (0·3 g.) in sulphuric acid (5 c.c.; *d* 1·84) and at 0° glacial acetic acid (30 c.c.) was added. After 30 minutes, the purple solution was poured into warm (60°) well-stirred absolute ethanol (150 c.c.) containing cuprous oxide (1·5 g.). After filtration, ethyl acetate and excess of ethanol were boiled off on the water-bath, and water (200 c.c.) was added. The solution was placed in the ice-chest, and after 12 hours the solid was removed, dried (in a vacuum), and crystallised repeatedly from ethanol (charcoal). The less soluble fraction furnished **2 : 4 : 7-*tribromotriazino*(4′ : 5′ : 6′-1 : 8*a* : 8)*naphthalene*,** (0·07 g.), m. p. 216—218° (decomp.) (Found : N, 9·9. $C_{10}H_4N_3Br_3$ requires N, 10·3%); the more soluble material gave, in minute yield, slightly impure **1 : 3 : 6**-tribromonaphthalene, m. p. 85—96° (Found : C, 34·1; H, 1·4; Br, 64·1%), undepressed on admixture with an authentic specimen. Examination of the two specimens by means of a polarising microscope showed that, as far as could be ascertained, they were identical.

The author gladly acknowledges Dr. H. H. Hodgson's permission further to develop investigations carried out with him at Huddersfield during 1943—44 and thanks him for his interest in this work. The author is also grateful to Mr. A. Stuart, Head of the Geology Department, University College, Exeter, for the examination of certain specimens with a polarising microscope, and to Professor L. Hunter of the University College, Leicester, for discussions. Thanks are also offered to the Council of the University College, Exeter, and Imperial Chemical Industries Limited for financial aid.

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48. *Degradation of α-Amino-acids by Interaction with Aldehydes.*

By Radwan Moubasher.

In his interpretation of the relative speed of the Strecker degradation of α-amino-acids by monocarbonyl compounds, Baddar (*J.*, 1949, S 163; 1950, 136) ignores steric considerations. The first step proposed, exemplified by $NH_2{\cdot}CHPh{\cdot}CO_2H + Ar{\cdot}CHO \longrightarrow Ar{\cdot}CH{:}N{\cdot}CHPh{\cdot}CO_2H$, is, however, strongly subject to steric hindrance (cf. Schonberg *et al.*, *J.*, 1950, 1422). Moreover, he defines as "active" substances which under severe conditions produce only traces of the degradation product. Again, contrary to Baddar's findings, piperonaldehyde degrades α-phenylglycine at approximately the same speed as does *m*-nitrobenzaldehyde. Baddar's explanation of the comparatively good yield of acetaldehyde obtained from *o*-nitrobenzaldehyde and alanine is questionable as according to him indigo, which is an active agent in the Strecker degradation, is formed in the process. His explanation of the relatively strong degrading power (in hot aqueous glycerol) of *s*-dichloroacetone, when compared with *o*-chlorobenzaldehyde, is also questionable since hydrochloric acid is formed on hydrolysis only in the former case, so that the experimental conditions are not equal in the two cases. His explanation of the mechanism of this degradation seems to be based on insufficient experimental evidence.

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[*Received, June 21st*, 1950.]

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49. *The Heat of Formation of Iodine Pentafluoride.*

By A. A. Woolf.

The determination of the heats of formation of certain halogen fluorides by utilizing their quantitative reactions with oxides has been suggested (Emeléus and Woolf, *J.*, 1950, 164). The heat evolved in the simplest of these reactions, the hydrolysis of iodine pentafluoride, has now been measured and leads to a value of 204·7 kcals. for the reaction $\frac{1}{2}I_2(s.) + 2\frac{1}{2}F_2(g.) = IF_5(l.)$ at 18°, and 194·6 kcals. for the reaction to yield the gaseous pentafluoride. The latent heat of vaporization, 10·1 kcals., was calculated from Ruff and Braida's vapour-pressure equation (*Z. anorg. allgem. Chem.*, 1933, **214**, 91).

A knowledge of the free energy of iodine pentafluoride will be useful in predicting whether certain fluorination reactions are possible with the liquid, but this must await the determination of its entropy. The heat of formation of bromine trifluoride, which cannot be determined by simple hydrolysis since the products of this reaction (bromine, oxygen, hydrobromic, and bromic acids) are formed in variable amounts, may be determined from the heat of the reaction $10BrF_3 + 3I_2 = 6IF_5 + 5Br_2$ now that the heat of formation of the pentafluoride is known.

Experimental.—Iodine pentafluoride, prepared from the elements at room temperature in a nickel apparatus, was decolorized immediately before use by fluorine, and purified by distillation at 20°/5 mm., a middle fraction (10 c.c. out of 40 c.c.) being collected.

The calorimeter, maintained at 20·0° in a thermostat, consisted of a 1·5-l. Dewar flask fitted with an insulated cover through which passed a calibration heater, ampoule holder and breaking rod, stirrer, and a Beckmann thermometer readable to 1/1000°. Sufficient iodine pentafluoride to produce a 1—2°-temperature rise was sealed in a Pyrex-glass ampoule, which was broken under 750 c.c. of water in the calorimeter. After the temperature rise due to the stirring had again become steady, a further one-degree rise was effected by applying a potential difference of 12 v. to the heater for 3 minutes.

The results are given below :—

IF_5/H_2O (mol. ratio)	1/1570	1/1190	1/888
Heat evolved per mol. of IF_5 (kcal.)	22·00	22·09	22·05
Mid-point of temperature rise	18·4°	18·7°	19·2°

The hydrolysis reaction, $IF_5 + 3H_2O = 5HF + HIO_3$, was first shown to occur quantitatively by Prideaux (*J.*, 1906, 316), and by using the following heats of formation (Bichowsky and Rossini, "Thermochemistry of Chemical Substances," Reinhold Publishing Corp., New York, 1936): H_2O 68·3(7), HF 75·5(6), and HIO_3 54·6 kcals., the heat of formation of iodine pentafluoride was calculated as 205·3 kcals.

The heat of mixing of iodic and hydrofluoric acids in the quantities resulting from the above hydrolysates was found by direct experiment to be negligible, and hence formation of difluoroiodic acid, if it occurred at all, had no thermal effect. The possibility of heat being evolved by attack on the Pyrex glass by the dilute hydrofluoric acid formed was also ruled out for the following reasons: (*a*) doubling the concentration of this acid did not alter the heat of hydrolysis within the estimated experimental error (1 in 250), (*b*) the temperature rise on hydrolysis reached its maximum value within 30 seconds (attack by hydrofluoric acid would not be instantaneous and a further rise in temperature would be expected), and (*c*) the attack on Pyrex glass by the hydrolysate in a period three times that of the above experiments was found by direct weighing to be negligible.

The heat of hydrolysis of the pentafluoride with N/4-potassium hydroxide was determined as a final check. The values found in duplicate experiments were 118·8 and 119·0 kcals., the increase in heat evolved as compared with aqueous hydrolysis being due to the heats of neutralization of the acids formed. From the equation $6KOH + IF_5 = 5KF + KIO_3 + 3H_2O$ by using the following heats of formation: KOH 114·8(0), KIO_3 114·7(7), and KF 138·3(9), the heat of formation of iodine pentafluoride was found to be 204·2 kcals. The difference between this figure and the one obtained in the aqueous hydrolysis is greater than experimental error and is probably due to errors in the heats of formation used. The heat of formation of iodic acid, 54·6 kcals., for example, is one chosen from a series which vary from 53·8 to 55·8 kcals. (Bichowsky and Rossini, *loc. cit.*).

The author is indebted to Professor H. J. Emeléus, F.R.S., for his encouragement, and to the Department of Scientific and Industrial Research for a maintenance grant.

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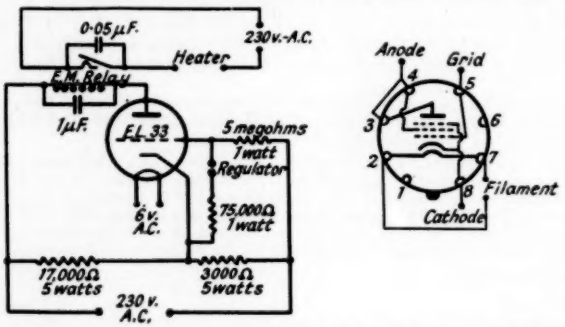
50. *An Inexpensive Thermostat Relay.*

By DUNCAN TAYLOR.

IT has become popular in recent years to employ some type of thyratron relay to afford accurate thermostatic control and to reduce the current at the mercury contact of the mercury–toluene regulator to not more than a few microamps. The regulator, therefore, provided that clean mercury is used for the initial filling, has a practically indefinite life, but not by any means can this be claimed for the thyratron valve. During recent studies in this Department on heterogeneous equilibria, accurate, continuous, and reliable thermostatic control was necessary for six months, and it was found that a thyratron relay could not be relied on to give more than, at most, three months' continuous service. To overcome this trouble, an inexpensive relay (see figure) was developed, and experience has shown that it combines all the desirable features of the thyratron type of relay with a useful life of six months' continuous running. Another good feature is that the thermostat heaters are cut off or switched on at the same instant as the regulator contacts close or open, respectively. The general principle involved in this relay is well established (cf. Cooke and Swallow, *J. Sci. Instr.*, 1929, **6**, 287), but the circuit illustrated has the advantage of operating from A.C. mains, uses inexpensive modern



components and requires no rectifier. The principle is simply that of an electromagnetic relay of the Post Office type in the anode circuit of a valve, the grid potential of which is varied by the opening and closing of the regulator contacts.

The electromagnetic relay should have a coil resistance of 1000 Ω and be fitted with heavy-duty normally-closed contacts (supplied for example by Londex Ltd., London, S.E.20). The relay will

function satisfactorily in this circuit if the contacts open smartly on the application of 10 v. D.C. to the coil. A 1-μF. condenser (750 v. D.C. test) must be connected across the relay coil to prevent continuous chatter, and a 0·05-μF. condenser (500 v. D.C. test) connected across the contacts is desirable though not essential as a spark suppressor when the contacts are interrupting a current of about 1 amp., *i.e.*, when using 250-w. heaters. There are no doubt several types of valve which could be used in this circuit, but the one preferred is a Mullard EL33, an ordinary radio output valve; this is rated to give a maximum anode current of about 33 ma., and in the circuit above the valve delivers only 13 ma. to the relay coil when the regulator closes. Under-running the valve in this way contributes to its long life on continuous usage. The connections to the valve are indicated in the figure. There is no difficulty in obtaining the necessary resistors, but it was convenient and less expensive to wind the 5-w. resistors from 41-S.W.G. enamelled resistance wire. The 230 v. A.C. to the network and the 6 v. A.C. to the valve can best be supplied from a small mains transformer.

When this circuit was being developed, it seemed at first sight preferable that the relay should work in the opposite way from that given in the figure, namely, that the relay coil should carry normally-open contacts which would close on energising of the coil by opening the regulator contacts. The circuit can in fact be arranged to operate in this manner, but then some instability is introduced, such that when current is flowing in the relay coil merely touching the regulator contacts with the fingers causes a large drop in current which may be sufficient to de-energise the coil. No such unpleasant features have been encountered in the circuit as given above.

Acknowledgments are due to Dr. R. Scott for some helpful discussions.

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51. *The Dissociation Constant of Calcium Hydroxide.*

By C. W. DAVIES and BERNARD E. HOYLE.

CALCIUM HYDROXIDE was shown to be incompletely dissociated in water by Kilde (*Z. anorg. Chem.*, 1934, **218**, 113), who obtained the value $K = 0{\cdot}04$ for the process $CaOH^{\cdot} \rightleftharpoons Ca^{\cdot\cdot} + OH'$ at 25°. This value was derived from measurements of the solubility of calcium iodate in alkaline solutions, and was subject to small corrections for the presence of $NaIO_3$ and $CaIO_3^{\cdot}$ ion pairs in the solutions studied; the revised value is $K = 0{\cdot}031$ (Davies, *J.*, 1938, 278). Recently, Bell and Prue (*J.*, 1949, 362) have obtained $K = 0{\cdot}051$ from measurements of the rate of decomposition of diacetone alcohol in calcium hydroxide solutions. The difference between the two values is of considerable interest, since the higher value is based on the assumption that only the free OH ion (and not the $CaOH^{\cdot}$ ion) catalyses the decomposition, and the discrepancy might be interpreted as indicating that this assumption is inaccurate. On the other hand, as Bell and Prue point out, Kilde's measurements were at relatively high ionic strengths so that part, at least, of the difference could be due to extrapolation errors.

The present note reports new measurements on the solubility of calcium iodate in calcium hydroxide solutions. These lead to $K = 0{\cdot}050$ for the second dissociation constant of calcium hydroxide, in agreement with Bell and Prue's value.

Calcium iodate hexahydrate was prepared, and its solubility measured, according to the methods described previously (*J.*, 1938, 273, 277). The calcium hydroxide was prepared from calcium carbonate "AnalaR," which was heated in a platinum crucible. The product, after cooling, was added to a suitable amount of carbon dioxide-free water, and the resulting solution was introduced into the saturator after the latter had been swept out with carbon dioxide-free air. When saturation had been attained, still in the absence of carbon dioxide, samples were withdrawn and rapidly titrated with 0·05N-hydrochloric acid, after which the iodate was estimated in the usual way. The experimental results are given in the first two columns of the table, which give the calcium hydroxide and iodate contents of the samples, both in millimols. per litre.

$Ca(OH)_2$.	$Ca(IO_3)_2$.	$CaIO_3^{\cdot}$.	$CaOH^{\cdot}$.	I.	K.	$Ca(OH)_2$.	$Ca(IO_3)_2$.	$CaIO_3^{\cdot}$.	$CaOH^{\cdot}$.	I.	K.
0	7·84	0·48	—	0·02256	—	14·26	6·42	0·68	3·67	0·05334	0·049
3·63	7·27	0·54	0·67	0·03028	0·050	15·13	6·37	0·69	3·90	0·05532	0·050
4·29	7·19	0·55	0·82	0·03170	0·049	18·60	6·23	0·72	5·25	0·06255	0·048
10·28	6·65	0·63	2·38	0·04477	0·050	20·93	6·15	0·74	6·20	0·06736	0·048
12·86	6·48	0·66	3·11	0·05048	0·051						

In addition to $Ca^{\cdot\cdot}$, IO_3', and OH' the solutions will contain $CaOH^{\cdot}$ and $CaIO_3^{\cdot}$. The dissociation constant of the latter is known ($K = 0{\cdot}13$), as is the solubility product of calcium iodate ($7{\cdot}119 \times 10^{-7}$). Activity coefficients were estimated from the equation:

$$-\log_{10} f_s = 0{\cdot}5z^2\{I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) - 0{\cdot}20I\} = 0{\cdot}5z^2 . F(I)$$

(Davies, *J.*, 1938, 2093), and by successive approximations the equations:

$$\log [Ca^{\cdot\cdot}][IO_3']/[CaIO_3^{\cdot}] = \log 0{\cdot}13 + 2F(I)$$

and $$\log [Ca^{++}][IO_3^-]^2 = \log S_0 + 3F(I)$$

were solved to give $[CaIO_3^+]$, $[Ca^{++}]$, and, by difference, $[CaOH^+]$. The calculations are summarised in Cols. 3, 4, and 5 of the table, and the dissociation constants given in the last column are obtained from

$$\log K_{CaOH} = \log [Ca^{++}][OH^-]/[CaOH^+] - 2F(I)$$

The most trustworthy K is probably given by the consistent results obtained in the more dilute solutions, since the slight falling off at the two highest ionic strengths might reflect increasing inaccuracy in the empirical activity equation used. This value, $K = 0{\cdot}050$, is in very good agreement with the value derived by Bell and Prue (*loc. cit.*; see also Bell and Waind, *J.*, 1950, 1979).

The solubility of calcium hydroxide in water at 25° is 0·020 mol./l. (Bassett, *J.*, 1934, 1270). Successive approximations based on the dissociation constant $K = 0{\cdot}050$ show that the saturated solution contains 5·00 millimols. per litre of the species $CaOH^+$; that is, one quarter of the calcium in a saturated lime solution is in this form.

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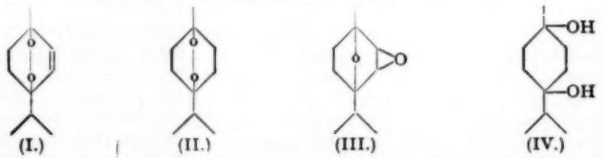
[*Received, September 12th*, 1950.]

52. *The Thermal Decomposition of Dihydroascaridole.*

By C. G. MOORE.

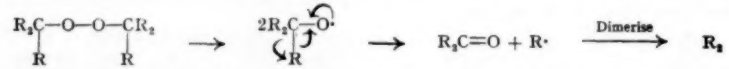
PAGET (*J.*, 1938, 829) has shown that when ascaridole (I) is partially hydrogenated in the presence of platinic oxide as catalyst the double bond is preferentially reduced giving dihydroascaridole (II) as the only product. This has now been confirmed by both quantitative micro-hydrogenation and partial macro-hydrogenation of the pure peroxide.



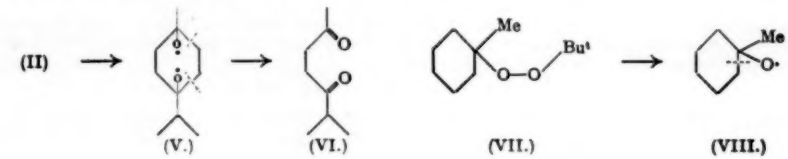
(I.) (II.) (III.) (IV.)

Dihydroascaridole, unlike ascaridole and the other known transannular peroxides, shows thermal stability. Thus ascaridole when heated alone at 130—150° decomposes violently with the evolution of combustible gases, chiefly propane (*Chem. Centr.*, 1908, I, 1839). It undergoes controlled decomposition to the isomeric dioxide (III) when heated at 130—150° in cymene (Nelson, *J. Amer. Chem. Soc.*, 1911, **33**, 1404; 1913, **35**, 84) and xylene (Henry and Paget, *J.*, 1921, 1714). In contrast to this it has now been found that dihydroascaridole is quantitatively recovered after being heated with *cyclo*hexene at 140° for 18 hours. Further, when heated in the liquid phase at 240°, dihydroascaridole decomposes non-explosively with the evolution of unidentified gaseous products and the formation of 6-methylheptane-2 : 5-dione (VI), together with a large amount of unidentified polymeric material.

These findings are relevent to the mode of thermal decomposition of di-*tert.*-alkyl peroxides (George and Walsh, *Trans. Faraday Soc.*, 1946, **42**, 94; Milas and Surgenor, *J. Amer. Chem. Soc.*, 1946, **68**, 205, 643; Milas and Perry, *ibid.*, 1938; Raley, Rust, and Vaughan, *ibid.*, 1948, **70**, 88), which when heated in the vapour phase undergo a homogeneous, first-order, non-chain, radical decomposition according to the following generalised scheme :



The formation of the diketone (VI) from dihydroascaridole, which may be regarded as a *cyclic* di-*tert.*-alkyl peroxide, can be accounted for in a similar way :



(V.) (VI.) (VII.) (VIII.)

It is noteworthy that in the diradical (V) the ring C–C bonds adjacent to the C–O bonds are broken in preference to the C–Me and C–Pr^i bonds. This accords with the fact that the peroxide (VII) yields the radical (VIII) which then breaks at a ring C–C bond in preference to the C–Me bond [Milas and Perry (*loc. cit.*); see also Walsh (*J.*, 1948, **331**, 398) for a general discussion of this subject].

The unreactivity of dihydroascaridole towards *cyclo*hexene at 140° contrasts with the considerable reaction of di-*tert.*-butyl peroxide with this olefin under similar conditions (Farmer and Moore, *J.*, 1951, **131**, **142**). In the latter case the *tert.*-butoxy-radicals, by virtue of their dehydrogenative capacity, effect a high degree of "dehydropolymerisation" of the olefin ($Bu^tO\cdot + RH \longrightarrow Bu^tOH + R\cdot$; $2R \longrightarrow R_2$, etc.). The *tert.*-butoxy-radicals undergo, in minor degree, decomposition to acetone and methyl radicals, and the latter may compete, to a small extent, with the *tert.*-butoxy-radicals in the dehydro-polymerisation reaction of the olefin.

The inertness of dihydroascaridole compared with di-*tert.*-butyl peroxide may be due to the greater dissociation energy of the cyclic-peroxide bond. Alternatively, homolytic fission of the O–O bonds may occur at comparable rates in both compounds, but the resulting radical units produced in (V), being held in close proximity by the *cyclo*hexane bridge, may have a marked tendency to recombine. Adverse steric factors may also operate to hinder effective collision between the *tert.*-alkoxy-radicals in (V) and olefin molecules.

The presence of the double bond in ascaridole probably acts in two ways as an important modifying influence in its thermal stability, compared with dihydroascaridole. Firstly, it presents a highly reactive site very close to the peroxide group. Secondly, as revealed by an examination of molecular models, it introduces additional strain in the C_6 ring and thence in the peroxide bond, thus making the steric factors considered above likely to be far less potent in influencing the reactivity of the radical units.

Experimental.—(Analyses by Dr. W. T. Chambers, Miss E. Farquhar, and Mrs. H. Hughes.) Ascaridole was freshly distilled before use, the fraction, b. p. 66—67°/1 mm., n_D^{15} 1·4752, being used (Found: C, 71·7; H, 9·6. Calc. for $C_{10}H_{16}O_2$: C, 71·4; H, 9·6%).

Quantitative hydrogenation of ascaridole. The peroxide (30·38 mg.) was hydrogenated in absolute ethanol (10·0 ml.), platinic oxide (10 mg.) being used as catalyst. 8·01 Ml. (N.T.P.) of hydrogen were absorbed, representing 98·8% of theory for complete reduction to *cis*-1 : 4-terpin (IV). The rate of hydrogenation shows that 1 mole of hydrogen per mole of peroxide is absorbed rapidly (*ca.* 5 minutes) and a second mole is absorbed more slowly taking a total of 18 hours for completion.

Dihydroascaridole. This was prepared essentially as described by Paget (*J.*, 1938, 829). It crystallised from cooled light petroleum (b. p. 40—60°) in large prisms, m. p. 19—20°, n_D^{18} 1·4690 (Found: C, 70·3; H, 10·65%; I.V., 0. Calc. for $C_{10}H_{18}O_2$: C, 70·6; H, 10·7%; I.V., 0).

Thermal decomposition of dihydroascaridole. (*a*) The peroxide (10·0 g.) was heated under an efficient reflux at an oil-bath temperature of 240° for 6 hours; a gaseous product (1·5 g.) was evolved. The liquid product (8·50 g.) on fractional distillation gave the fractions: (i) (3·1 g.), b. p. 79—82°/9 mm.; (ii) unchanged peroxide (1·4 g.), b. p. 104—106°/10 mm.; and (iii) a dark-brown viscous polymeric residue (*ca.* 4·0 g.) which was not further investigated. Fraction (i) was identified as 6-methylheptane-2 : 5-dione (VI), n_D^{20} 1·4322 (Found: C, 67·7; H, 9·85. Calc. for $C_8H_{14}O_2$: C, 67·55; H, 9·9%). Semmler (*Ber.*, 1909, **42**, 522) gives b. p. 82—86°/10 mm.; n_D 1·433; von Auwers and Hinterseber (*Ber.*, 1915, **48**, 1357) give b. p. 90—91°/16 mm., n_D^{20} 1·4330. The diketone gave a dioxime which crystallised from acetone in rectangular prisms, m. p. 137° (Found: C, 55·95; H, 9·5; N, 16·25. Calc. for $C_8H_{16}O_2N_2$: C, 55·8; H, 9·35; N, 16·3%). Wallach and Meister (*Annalen*, **362**, 264) and Ciamician and Silber (*Ber.*, 1913, **46**, 3077) record m. p. 137°. The semicarbazide derivative (2-methyl-5-*iso*propyl-1-ureidopyrrole) separated from absolute ethanol in micro-crystals, m. p. 199—200°. Ciamician and Silber (*loc. cit.*) record m. p. 201°.

(*b*) A mixture of the peroxide (8·2 g.) and *cyclo*hexene (45·0 g.) was heated in a nitrogen-filled sealed tube at 140° for 18 hours. Fractionation of the product (53·2 g.) gave *cyclo*hexene, b. p. 83—84°, and unchanged dihydroascaridole (8·2 g., 100%), b. p. 58—60°/1 mm., n_D^{15} 1·4690, m. p. 18—19° (Found: C, 70·85; H, 10·6%). Its identity as the unchanged peroxide was further confirmed by catalytic hydrogenation (in ethanol over palladium–charcoal) whereupon *cis*-1 : 4-terpin (96%), m. p. 117° (Found: C, 70·2; H, 11·9. Calc. for $C_{10}H_{20}O_2$: C, 69·7; H, 11·7%), was obtained.

BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48/52, TEWIN ROAD, WELWYN GARDEN CITY, HERTS.

[*Received, September 18th*, 1950.]

53. *The Reaction of Di-*tert.*-butyl Peroxide with Butan-2-one and cyclo*Hexanone.*

By C. G. Moore.

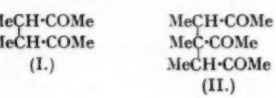
It has been shown previously (Farmer and Moore, *J.*, **1951**, **131**, **142**; Raley, Rust, Seubold, and Vaughan, *J. Amer. Chem. Soc.*, **1948**, **70**, 88, 95, 1336) that *tert.*-butoxy-radicals formed by the liquid-phase thermal decomposition at 140° of di-*tert.*-butyl peroxide are highly effective agents for the "dehydro-polymerisation" of olefins, paraffins, and alkylbenzenes. The *tert.*-butoxy-radicals display a highly selective action, being utilised almost entirely in abstracting α-methylenic hydrogen atoms of the hydrocarbon to form *tert.*-butanol and a hydrocarbon radical which is stabilised by dimerisation:

$$RH + Bu^tO\cdot \longrightarrow R\cdot + Bu^tOH;\ 2R\cdot \longrightarrow R_2$$

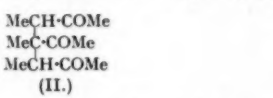
The *tert.*-butoxy-radicals decompose in small degree under these conditions to give acetone and methyl radicals and the latter compete, to a small extent, with the former in the dehydro-polymerisation of the hydrocarbon solvent:

$$Bu^tO\cdot \longrightarrow (CH_3)_2C{:}O + CH_3\cdot;\ CH_3\cdot + RH \longrightarrow CH_4 + R\cdot;\ 2R\cdot \longrightarrow R_2$$

Di-*tert.*-butyl peroxide has now been shown to be a highly effective reagent for the cross-linking of cyclic and acyclic monoketones at the α-methylenic position giving 1 : 4-diketones and, by subsequent reaction of the peroxide with the primary reaction product, higher "dehydro-polymeric" ketones. Thus, heating the peroxide with a large excess of butan-2-one at 140° gave a mixture of ketonic "polymers," which on distillation gave: (i) pure 3 : 4-dimethylhexane-2 : 5-dione (I) (50·7% of the "polymer"), (ii) a slightly impure triketone, presumably (II) (10·7%), and (iii) a residue (38·6%), consisting of higher ketonic "dehydro-polymers."



(I.)



(II.)

Similarly, *cyclo*hexanone when heated with the peroxide at 140—150° gave, in addition to a mixture of approximately tetrameric ketone "polymers," a mixture of the two stereoisomeric 2 : 2′-diketodi*cyclo*hexyls from which the higher-melting form (m. p. 73—74°) was separated. This ketone has been synthesised by unambiguous means by Plant (*J.*, 1930, 1595).

After completion of this work, Kharasch, McBay, and Urry (*J. Amer. Chem. Soc.*, 1948, **70**, 1269) published analogous findings of a similar, but more detailed, study of the action of free methyl radicals, derived from diacetyl peroxide, on a large number of aliphatic ketones. A common mechanism is regarded as being operative in both cases:

$$RCO\cdot CH_2R' + \underset{[CH_3\cdot]}{Bu^tO\cdot} \longrightarrow RCO\cdot\dot{C}HR' + \underset{[CH_4]}{Bu^tOH};\ 2RCO\cdot\dot{C}HR' \longrightarrow \begin{matrix} RCO\cdot CHR' \\ | \\ RCO\cdot CHR' \end{matrix}$$

(III.)

That the *tert.*-butoxy-radicals are in the present instance the major dehydrogenative agents is shown by the high yield of *tert.*-butanol (≯79% of the peroxide decomposed) obtained in the reaction with *cyclo*hexanone and by the absence of any appreciable gaseous products (methane and ethane) in the reaction with butan-2-one.

Provided the "dehydro-dimer" (III) still possesses α-methylenic hydrogen atoms it will compete with the monomeric ketone for reaction with *tert.*-butoxy-radicals, so giving the observed "dehydro-trimers," etc.

This same parallelism of action of methyl and *tert.*-butoxy-radicals exists in their abilities to produce α-methylenic carbon–carbon cross-linking in alkylbenzenes (Kharasch *et al.*, *J. Org. Chem.*, **1945**, **10**, 401; Farmer and Moore, *loc. cit.*) and olefins (Farmer and Moore, *loc. cit.*; Koch, *J.*, 1948, 1111).

The present demonstration that (I) is the sole diketone isolated from the reaction of butan-2-one with di-*tert.*-butyl peroxide, and the formation of substantial amounts of "polymeric" ketones in this reaction, despite the large excess of butan-2-one used, confirm Kharasch, McBay, and Urry's observations (*loc. cit.*) and support the conclusion of many

workers that the relative susceptibilities to radical attack of primary, secondary, and tertiary C–H α-methylenic bonds is in the direction $C^t—H > C^s—H > C^p—H$.

Experimental.—(Analyses by Dr. W. T. Chambers, Miss E. Farquhar, and Mrs. H. Hughes.)

*Reaction of butan-2-one with di-*tert.*-butyl peroxide.* A mixture of the ketone (72 g.) and the peroxide (36·5 g.) was heated in evacuated sealed tubes at 140° for 24 hours. Fractionation of the product gave: (i) b. p. 73—80°/760 mm. (78·65 g.), being a mixture of *tert.*-butanol and unreacted ketone; (ii) a small intermediate fraction, b. p. <74°/8 mm. (0·94 g.); (iii) b. p. 74—76°/8 mm., n_D^{20} 1·4342 (11·55 g.); (iv) a viscous orange liquid, b. p. 76—84°/1 mm., n_D^{20} 1·4651 (2·45 g.), and (v) a dark-orange residue (8·8 g.).

Fraction (iii) was 3 : 4-dimethylhexane-2 : 5-dione [Found: C, 67·6; H, 9·9; *M* (ebullioscopic, in acetone), 138 ± 12. Calc. for $C_8H_{14}O_2$: C, 67·6; H, 9·9%; *M*, 142]. It gave a dioxime monohydrate which crystallised from aqueous ethanol in needles, m. p. 200—201° (Found: C, 50·7; H, 9·7; N, 14·5. Calc. for $C_8H_{14}O_2N_2.H_2O$: C, 50·5; H, 9·55; N, 14·75%. Found, in a sample heated at 100—120° *in vacuo*: C, 55·95; H, 9·45; N, 16·1. Calc. for $C_8H_{16}O_2N_2$: C, 55·8; H, 9·3; N, 16·3%). Ciamician and Silber (*Ber.*, 1912, **45**, 1540) give m. p. 202°. Treatment of the diketone with phenylhydrazine in aqueous acetic acid gave 1 : 2-dihydro-3 : 4 : 5 : 6-tetramethyl-1-phenylpyridazine, which crystallised from aqueous ethanol in needles, m. p. 126—127° (Found: C, 78·5; H, 8·5; N, 12·9. Calc. for $C_{14}H_{18}N_2$: C, 78·5; H, 8·4; N, 13·1%). Ciamician and Silber (*loc. cit.*) give m. p. 130°; Kharasch *et al.* (*J. Amer. Chem. Soc.*, 1948, **70**, 1269) give m. p. 127—128°.

Fraction (iv) was a slightly impure "trimeric" *ketone*, presumably (II) [Found: C, 68·6; H, 9·5; *M* (ebullioscopic, in acetone), 215 ± 24. $C_{12}H_{20}O_3$ requires C, 67·95; H, 9·45; *M*, 212]. Although the liquid gave a positive reaction with aqueous 2 : 4-dinitrophenylhydrazine sulphate no pure derivative could be obtained, nor could a pure oxime be prepared under the usual conditions.

Reaction of cyclo*hexanone with di-*tert.*-butyl peroxide.* The ketone (98 g.; b. p. 56—56·5°/20 mm., n_D^{20} 1·4508) and the peroxide (24·4 g.) were heated under reflux at 140—150° for 48 hours. On distillation, the product, a bright red liquid, gave the fractions: (i) *tert.*-butanol, b. p. 80—83°/763 mm. (17·6 g.); (ii) unreacted peroxide, b. p. 110°/763 mm. (2·5 g.); (iii) unchanged *cyclo*hexanone, b. p. 48—50°/13 mm. (82·4 g.); and a higher-boiling material (13·1 g.), from which were obtained (iv) b. p. 117—120° mm. (5·0 g.), and an undistillable residue (*ca.* 8·0 g.) which set, on cooling, to a bright-orange resin.

Redistillation of (iv) gave a mixture of the two stereoisomeric 2 : 2′-diketodi*cyclo*hexyls as an oil b. p. 110—117° (mainly 116—117°)/1 mm., n_D^{20} 1·4999 (Found: C, 74·2; H, 9·4. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·35%). On being cooled in solid carbon dioxide the oil partially crystallised. The solid, when separated and crystallised from light petroleum (b. p. 40—60°), gave the higher-melting form as long prismatic needles, m. p. 73—74° (Found: C, 74·2; H, 9·35%). Both Plant (*loc. cit.*) and Kharasch *et al.* (*J. Amer. Chem. Soc.*, 1948, **70**, 1269) give m. p. 70—71°.

The residue was shown to have the average composition of a *cyclo*hexanone "*dehydro-tetramer*" [Found: C, 76·7, 76·1; H, 8·9, 8·65; *M* (ebullioscopic, in benzene), 360, 370. $C_{24}H_{34}O_4$ requires C, 74·6; H, 8·9%; *M*, 286].

THE BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48, TEWIN ROAD, WELWYN GARDEN CITY, HERTS. [*Received, September 18th*, 1950.]

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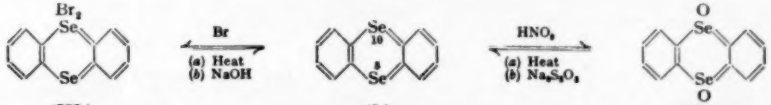
54. *Some Derivatives of Selenanthren.*

By N. M. CULLINANE.

BY treatment of selenanthren (I) with nitric acid Krafft and Kaschau (*Ber.*, 1896, **29**, 443) obtained a dioxide which melted at 270° (decomp.). In the present work a product melting at 265° (decomp.), presumably the same compound, was obtained, but, in addition, a small quantity of material melting at 249° (decomp.); the latter may be a stereoisomeric form of the former.

Selenanthren 5 : 10-dioxide (II), which crystallises from water as a hydrate—a phenomenon also observed in similar compounds, *e.g.*, diphenyl selenoxide (Banks and Hamilton, *J. Amer. Chem. Soc.*, 1939, **61**, 2306) and phenoxselenin (Drew, *J.*, 1928, 511)—is reconverted into the parent substance by heating it to its melting point or treating it with sodium pyrosulphite; thus it is not the 5 : 5-dioxide which would not be reduced by such processes.



(III.) (I.) (II.)

Whereas diphenyl selenoxide (Krafft and Vorster, *Ber.*, 1893, **26**, 2813) and thianthren 5-oxide (Fries and Vogt, *Annalen*, 1911, **381**, 326) both yield dichlorides on treatment with

hydrochloric acid, selenanthren 5 : 10-dioxide readily forms a dihydrochloride; there appears to be no other record of selenoxides reacting with hydrochloric acid in this way.

In general selenoxides are not easily oxidised to selenones (Gaythwaite, Kenyon, and Phillips, *J.*, 1928, 2280) and it was not possible to convert selenanthren 5 : 10-dioxide into a selenone.

Bromine converts selenanthren into the dibromide, which probably has the structure (III), an unstable substance which regenerates selenanthren when it is kept in air, heated, or treated with sodium hydroxide.

Experimental.—Selenanthren 5 : 10-*dioxide.* Selenanthren was prepared by heating a mixture of thianthren tetroxide and selenium (Krafft and Kaschau, *loc. cit.*; Cullinane, Rees, and Plummer, *J.*, 1939, 151); its m. p. was 180°. It gradually dissolved in concentrated sulphuric acid, the liquid becoming blue-violet, then deep blue, and finally pale blue. Ferric chloride or syrupy phosphoric acid gave no colour (contrast thianthren).

The method of oxidation was a modification of that used by Krafft and Kaschau. To finely powdered selenanthren (8 g.) nitric acid (*d* 1·2; 230 c.c.) was added and the whole was boiled until evolution of brown fumes had ceased (about 15 minutes). Excess of 2N-sodium hydroxide was introduced and the whole kept for 12 hours in a stoppered flask, whereafter it was made acid by passing in carbon dioxide. The water was then completely driven off *in vacuo* at a low temperature, and the solid extracted with a large volume of boiling alcohol, on evaporation of which the dioxide, mixed with a little sodium carbonate, remained. After being washed with small portions of water the dioxide (6 g.) was obtained. It crystallised from hot water, in which it was moderately soluble, in colourless plates with water of crystallisation which was removed at 130° during 3 hours. The first crop of crystals separating from the aqueous solution consisted of plates, in very small amount, which after being heated at 130° to constant weight decomposed sharply at 249° with loss of oxygen and complete conversion into selenanthren. The main product from the mother liquors melted at 265° with rapid decomposition to selenanthren. It was slightly soluble in ethanol, somewhat more in acetic acid, and insoluble in carbon disulphide or benzene [Found (compound, m. p. 265°): C, 42·2, H, 2·4. (Compound, m. p. 249°): C, 42·2, H, 2·4. $C_{12}H_8O_2Se_2$ requires C, 42·1, H, 2·3%].

Addition of concentrated sulphuric acid caused the crystals to become bluish-violet, then as they slowly dissolved the solution became reddish-violet; when heated, the solution became purplish-red, and then pink on storage. Further heating caused the colour to become purple and finally violet. In syrupy phosphoric acid the dioxide gave a pale pink solution, gradually becoming pale blue.

Treatment of selenanthren in acetic solution with excess of perhydrol gave only a very small yield of the dioxide, most of the initial material being recovered. The dioxide could not be oxidised to a selenone by perhydrol or chromic acid.

Conversion of selenanthren dioxide into selenanthren. Selenanthren was obtained in quantitative yield when the dioxide was heated to its m. p. and when it was ground in a mortar with a concentrated solution of sodium pyrosulphite and then kept with occasional shaking for 12 hours in a stoppered bottle, and the product was washed with water and crystallised from carbon disulphide.

Selenanthren dioxide dihydrochloride. A solution of the dioxide in hot water was cooled to about 35° and then, before precipitation occurred, excess of concentrated hydrochloric acid was added rapidly. Immediately a copious white precipitate was formed; the *salt* was quickly dried and melted at 213° with brisk decomposition (Found: Cl, 17·3, 17·0. $C_{12}H_8O_2Se_2,2HCl$ requires Cl, 17·1%).

Selenanthren dibromide. To a solution of selenanthren (1·7 g.) in carbon disulphide (20 c.c.) bromine (1·2 g., 1·5 mols.) was slowly added with shaking and cooling. Crystals separated during the addition. After 30 minutes the *dibromide* was collected and washed with dry carbon disulphide; it formed brownish-red prisms, m. p. 140° (decomp.) (Found: Br, 34·9. $C_{12}H_8Se_2Br_2$ requires Br, 34·0%), and gave with concentrated sulphuric acid a rose-pink colour, which gradually became purplish-pink, purple, permanganate-coloured, and finally deep blue. On addition of dilute aqueous sodium hydroxide the crystals became white, the process being accelerated by rubbing; the product was extracted with hot water, from which a very small quantity of the dioxide was isolated; the residue was taken up in carbon disulphide and found to consist of selenanthren (yield over 90%). When kept in air or heated the dibromide was eventually transformed entirely into selenanthren.

THE TATEM LABORATORIES, UNIVERSITY COLLEGE,
CARDIFF.

[*Received, October 4th*, 1950.]

THE CHEMICAL SOCIETY

SCIENTIFIC MEETINGS DURING FEBRUARY, 1951

LONDON.

Thursday, February 1st, 1951, at 7.30 p.m.

The following papers will be read and discussed:

"Experiments on the Synthesis of the Pyrethrins. Part VI. Synthesis of *trans*-Pyrethrone and *trans*-Pyrethrolone." By L. Crombie, S. H. Harper, and D. Thompson.

"Synthetic Long-chain Aliphatic Compounds. Part III. A Critical Examination of Two Methods of Olefinic Acid Synthesis." By D. E. Ames and R. E. Bowman.

"The Synthesis of Sugars from Simpler Compounds. Part I. The *in vitro* Synthesis of the Pentoses." By L. Hough and J. K. N. Jones.

Thursday, February 15th, 1951, at 7.30 p.m.

Tilden Lecture, **Atoms and Radicals in Aqueous Solution,** by Professor F. S. Dainton, M.A., Ph.D.

ABERDEEN.

Thursday, February 22nd, 1951, at 7.30 p.m.

Lecture, **Ion Exchange in Crystals**, by Professor R. M. Barrer, D.Sc., F.R.I.C.

Joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry to be held in the Chemistry Department, Marischal College, Aberdeen.

BRISTOL.

Wednesday, February 7th, 1951, at 7 p.m.

Lecture, **Some Aspects of Polysaccharide Chemistry,** by Dr. J. K. N. Jones, A.R.I.C.

Joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry to be held at Gloucester Technical College.

Thursday, February 8th, 1951, at 7 p.m.

Lecture, **The Structural Relationships in the Group of Cell-wall Polysaccharides,** by Professor E. L. Hirst, M.A., Ph.D., F.R.S.

Joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry to be held in the Chemistry Department, The University, Bristol.

EDINBURGH.

Tuesday, February 6th, 1951, at 7 p.m.

Lecture, **Application of Exothermic Solid Reactions to Jet Propulsion and Industrial Purposes,** by Dr. J. Taylor.

Joint meeting with the University Chemical Society, the Royal Institute of Chemistry, and the Society of Chemical Industry to be held in the Biochemistry Lecture Theatre, The University, Edinburgh.

Thursday, February 22nd, 1951, at 7.30 p.m.

Lecture, **Some Aspects of Infra-red Measurements,** by Dr. H. W. Thompson, M.A., F.R.S.

Joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry to be held at the North British Station Hotel, Edinburgh.

EXETER.

Monday, February 5th, 1951, at 5 p.m.

Lecture, **The Chemistry of Carbon and Silicon**, by Professor E. D. Hughes, D.Sc., F.R.S.

To be given in the Washington Singer Laboratories, Prince of Wales Road, Exeter.

GLASGOW.

Friday, February 16th, 1951, at 7 p.m.

Annual General Meeting of Local Fellows. 7.15 p.m. Meeting for the reading of original papers.

To be held in the Royal Technical College, Glasgow.

HULL.

Thursday, February 1st, 1951, at 6 p.m.

Lecture, **The Comparative Chemistry of Carbon and Silicon,** by Professor E. D. Hughes, D.Sc., F.R.S.

Joint meeting with University College Scientific Society to be held in the Science Lecture Theatre, University College, Hull.

LIVERPOOL.

Thursday, February 8th, 1951, at 4.30 p.m.

Lecture, **Some Recent Developments in Photochemistry,** by Professor R. G. W. Norrish, Sc.D., F.R.S.

Joint meeting with the Royal Institute of Chemistry, the Society of Chemical Industry, and the British Association of Chemists to be held in the Chemistry Lecture Theatre, The University, Liverpool.

MANCHESTER.

Thursday, February 15th, 1951, at 6.30 p.m.

Meeting for the reading of original papers.

To be held in the University, Manchester.

NEWCASTLE AND DURHAM.

Friday, February 23rd, 1951, at 5 p.m.

Bedson Club Lecture, **Metabolic Products of Moulds,** by Professor A. Robertson, M.A., Ph.D., F.R.S.

To be given in the Chemistry Building, King's College, Newcastle-on-Tyne. All Fellows are invited.

NORTHERN IRELAND.

Wednesday, February 7th, 1951, at 7.30 p.m.

Lecture, **A New Monomer : Acenaphthylene, its Polymers and Co-polymers,** by Mr. A. Fowler Williams, M.Sc., A.R.I.C., and Mr. M. Kaufman, B.Sc., A.R.I.C.

Joint meeting with the Royal Institute of Chemistry and the Plastics Group of the Society of Chemical Industry to be held in the Lecture Theatre, Department of Agriculture, Belfast.

NORTH WALES.

Thursday, February 1st, 1951, at 5.45 p.m.

Lecture, **What is a Chemical Bond ?** by Professor C. A. Coulson, M.A., D.Sc., F.R.S.

Joint meeting with the University College of North Wales Chemical Society and the University of Liverpool Chemical Society to be held in the Department of Chemistry, University College of North Wales, Bangor.

NOTTINGHAM.

Thursday, February 8th, 1951, at 6.30 p.m.

Lecture, **Organic Syntheses at Anodes,** by Professor R. P. Linstead, C.B.E., D.Sc., F.R.S.

Joint meeting with the University Chemical Society to be held in the Chemistry Lecture Theatre, The University, Nottingham.

Thursday, February 22nd, 1951, at 6.30 p.m.

Lecture, **The Breakdown of Macromolecules,** by Professor H. W. Melville, D.Sc., F.R.S.

Joint meeting with the University Chemical Society to be held in the Chemistry Lecture Theatre, The University, Nottingham.

ST. ANDREWS AND DUNDEE.

Thursday, February 8th, 1951, at 5.15 p.m.

Lecture, **Radio Waves from the Sun and Stars,** by Sir Edward Appleton, K.C.B., C.B.E., F.R.S.

Joint meeting under the auspices of the British Association (Dundee) Trust to be held in the Chemistry Department, University College, Dundee.

Friday, February 9th, 1951, at 5.15 p.m.

Lecture, **The Formation and Reactions of Free Radicals produced by Photo-excitation,** by Professor M. G. Evans, D.Sc., F.R.S.

Joint meeting with St. Andrews University Chemical Society to be held in the Chemistry Department, United College, St. Andrews.

Thursday, February 15th, 1951, at 5.15 p.m.

Frankland Memorial Lecture, **Structural Chemistry,** by Professor W. Wardlaw, C.B.E., D.Sc., F.R.I.C.

To be given in the Chemistry Department, University College, Dundee.

Friday, February 23rd, 1951, at 5.15 p.m.

Lecture, **Some Recent Aspects of Infra-red Measurements,** by Dr. H. W. Thompson, M.A., F.R.S.

Joint meeting with St. Andrews University Chemical Society to be held in the Chemistry Department, United College, St. Andrews.

SHEFFIELD.

Thursday, February 1st, 1951, at 5.30 p.m.

Lecture, **Catalysed Oxidations,** by Professor C. E. H. Bawn, Ph.D.

Joint meeting with the University Chemical Society to be held in the Chemistry Lecture Theatre, The University, Sheffield.

SOUTHAMPTON.

Friday, February 23rd, 1951, at 5 p.m.

Lecture, **What is a Chemical Bond?** by Professor C. A. Coulson, M.A., D.Sc., F.R.S.

Joint meeting with Southampton University College Chemical Society to be held in the Physics Department, University College, Southampton.

SOUTH WALES.

Friday, February 2nd, 1951, at 5.30 p.m.

Lecture, **What is a Chemical Bond?** by Professor C. A. Coulson, M.A., D.Sc., F.R.S.

Joint meeting with University College of Swansea Chemical Society to be held at University College, Swansea.

PROCEEDINGS

OF THE

CHEMICAL SOCIETY.

Minutes of a

SCIENTIFIC MEETING

held in the Dobbie Lecture Theatre, University College of North Wales, Bangor, on Thursday, November 23rd, 1950, at 5.45 p.m.

PROFESSOR S. PEAT, on behalf of the University College of North Wales, and His Worship the Mayor of Bangor, on behalf of the City, welcomed the Society on the occasion of the first Official Meeting to be held in the North Wales area. The Chair was then taken by PROFESSOR R. P. LINSTEAD, C.B.E., D.Sc., F.R.S., Vice-President, who replied on behalf of the Society.

FORMAL ADMISSION OF FELLOWS.

The following were admitted Fellows of the Society: Glyn O. Phillips, J. M. Bailey, D. M. Jones, Gwen J. Thomas, D. J. McGilvray, Rowland A. Evans, J. Dewi Jones, F. H. Newth, M. G. Lines, M. J. Rose, E. W. Bodycote, A. M. Spivey, J. A. R. Bates, G. H. Nancollas, R. S. Finlow.

TILDEN LECTURE.

The Chairman called upon Dr. F. L. Rose, O.B.E., to deliver the Tilden Lecture entitled "A Chemotherapeutic Search in Retrospect." At the conclusion of the Lecture, a vote of thanks to Dr. Rose, proposed by Dr. W. R. Angus, was carried with acclamation.

Minutes of a

SCIENTIFIC MEETING

held at Burlington House, London, W.1, on Thursday, December 14th, 1950, at 7.30 p.m.

The President, PROFESSOR E. K. RIDEAL, M.B.E., M.A., D.Sc., F.R.S., was in the Chair.

MINUTES.

The Minutes of the Scientific Meetings held at Burlington House, University College, Southampton, and University College of North Wales, Bangor, on November 16th, 17th, and 23rd respectively were read, and were confirmed and signed.

FORMAL ADMISSION OF FELLOWS.

The following were admitted Fellows of the Society: Ingrid G. Roe, D. Reichenberg, D. F. Muggleton, A. D. Baynes Cope, L. Turner, E. D. White, Brian G. Baldwin, R. J. Callow.

SCIENTIFIC COMMUNICATIONS.

The following papers were read and discussed:

"The Oxidation of *n*-Decaldehyde." By H. R. Cooper and H. W. Melville.

"Contributions to the Hydrothermal Chemistry of Silicates. Part I." By R. M. Barrer and E. A. D. White.

"Some Comments on Brunauer, Emmett, and Teller's Adsorption Equation." By D. C. Jones.

OFFICIAL ANNOUNCEMENTS

DEATHS.

The Council regret to announce the deaths of the following Fellows :

	Elected.	Died.
George Dixon (St. Bees)	June 7th, 1894.	Oct. 21st, 1950.
John Duncan (Sydney, N.S.W.)	Feb. 15th, 1912.	Aug. 10th, 1950.
William Thomas Wright (Sheffield)	Mar. 4th, 1886.	July 17th, 1950.

CONGRATULATIONS—SIXTY AND FIFTY YEARS OF FELLOWSHIP.

The President has conveyed the congratulations of the Society to John Joseph Sudborough (Torquay) who completed 60 years of Fellowship on December 4th, 1950, and to the following who completed 50 years of Fellowship on December 6th, 1950 :

Theodore Ridley Burnett (Dumfries).
Alexander Davidson (Co. Wicklow).
George Harker (Sydney).
Thomas Marginson Nightingale (Bolton).
Henry Ernest Stapleton (Jersey).

ELECTION OF NEW FELLOWS.

The following 49 candidates were elected Fellows of the Society on December 14th, 1950 :

Samuel Rusmisell Aspinall.
Bernard Douglas Astill.
Philip William Barlow.
Terence Neil Belford.
Michael Camm Bennett.
Derek Blair.
John Bernard Brown.
Michael William Buxton.
Charles Arnold Coleman-Porter.
Albert John Crocker.
Robert Frank Curtis.
Glyn Davies.
Bernard Ernest Dawson.
Herman Johannes Den Hertog.
David Frank Exley.
Erich Karl Franz Friedrich Foerster.
Francis Paul Gintz.
Ronald Grime.
Geoffrey Linton Hardy.
Howard Eugene Heller.
Dylla Esther Mabel Hosking.
Geoffrey Baldwin Jackman.
Georges July.
Morris S. Kharasch.
David Neville Kirk.
Dennis Holden Laney.
Richard David Langstaff.
John Arthur Law.
Alan James Lemin.
Jean Victoria Louise Longstaff.
Leslie Frederick Alfred Mason.
Kunj Behari Lal Mathur.
James Kenneth Myatt.
Walter Nudenberg.
Roland Burnand Page.
Alan Ernest Owen.
Joseph Adeodatus Kwatekwei Quartey.
Harry Rosenberg.
George William Ross.
John Thomas Rundquist.
John Robert Russell.
Leonard Salmon.
Alfred Edward Shaw.
Michael Arthur Short.
Ronald Edwin Stedman.
Edward Curtis Taylor, jun.
Leon Edward Tenenbaum.
Raymond Todd.
Ronald Henry Vickers.

GIFTS.

Acknowledgment is made of a gift towards the cost of publications from Mr. D. Holmes and of a gift of the Society's publications from Lobitos Oil Fields, Ltd.

HARRISON MEMORIAL PRIZE.

The Harrison Memorial Prize Selection Committee has awarded the Harrison Memorial Prize for 1950 to Dr. Hugh Christopher Longuet-Higgins of the University of Manchester. The Presentation will be made during the Anniversary Meetings to be held in March 1951.

ACCOMMODATION.

The President has been appointed to serve on the Scientific Societies Accommodation Committee of the Royal Society to advise on the co-ordination of the accommodation requirements of scientific societies in the proposed science centre.

INTERNATIONAL ATOMIC WEIGHTS.

A table of Atomic Weights, reprinted from the 15th Report of the Committee on Atomic Weights of the International Union of Chemistry, is published in the *Journal* for January, 1951, p. 1. Copies of the table, printed on card, may be obtained from the General Secretary, price one shilling each, post free.

MEETINGS OUTSIDE LONDON.

EDINBURGH.

" Homolytic Aromatic Substitution," by Professor D. H. Hey, D.Sc., F.R.I.C.

A joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry was held at the North British Station Hotel on November 23rd, 1950, with Dr. Neil Campbell in the Chair.

Professor Hey delivered a most interesting lecture, and a vote of thanks, moved by Dr. Duncan Taylor, was carried with acclamation.

SHEFFIELD.

" New Ventures in Carbohydrate Chemistry," by Professor M. Stacey, D.Sc., F.R.S.

A joint meeting with the University Chemical Society was held in the Chemistry Lecture Theatre of the University on November 30th, 1950, with Professor R. D. Haworth in the Chair.

Professor Stacey gave a review of recent developments, mentioning such diverse topics as paper chromatography, methylation by means of sodamide, new blocking groups (*e.g.*, trifluoroacetyl), the use of sucrose as a raw material for chemical synthesis, ethylene oxide sugars, deoxy-sugars, enzymic syntheses, and the use of partly depolymerised dextran as a substitute for blood plasma. On the motion of Dr. A. H. Lamberton a hearty vote of thanks was given to the Lecturer.

LIST OF APPLICATIONS FOR FELLOWSHIP

(*Fellows wishing to lodge objection to the election of these candidates should communicate with the Honorary Secretaries within ten days of the date of publication of the* Journal *for January, 1951. Such objections will be treated as confidential. The forms of applications are available in the Library.*)

***Allen, Joseph Frederick.** British. c/o Mrs. Dawson, 20, Luccombe Place, Shirley, Southampton. Student, University College, Southampton. *Signed by:* E. Cartmell, K. R. Webb, I. G. M. Campbell.

Aparicio, Fidel Jorge Lopez, D.Chem. (Madrid). Spanish. Balliol College, Oxford. Research Student. *Signed by:* W. A. Waters, Ivan M. Roitt, J. A. Alexander.

***Avery, Michael John,** B.Sc. (Lond.). British. 86, Ingram Road, Thornton Heath. National Service. *Signed by:* J. V. Westwood, D. B. Powell, D. W. Wilson.

Baigent, Alfred Edwin Philip. British. Orchard Paddock, Kilcot, Newent. Works Manager, J. M. Collett & Co., Ltd., Gloucester. *Signed by:* E. W. Cornwell, R. E. Tebbit, F. J. Green, C. A. Hawkes.

***Barnard, Peter William Cecil.** British. 12, St. Leonards Avenue, Windsor. Student, University College, London. *Signed by:* H. G. Poole, O. L. Brady, Henry Terrey.

Barnes, Charles Stalley, M.Sc. (Adelaide). British. Division of Industrial Chemistry, C.S.I.R.O., Box 4331 G.P.O., Melbourne, Victoria. Research Officer. *Signed by:* R. G. Curtis, H. Duewell, H. H. Hatt.

Barnes, Sidney Charles, A.R.I.C. British. 343, London Road, Appleton, Nr. Warrington. Chief Assistant to Public Analyst. *Signed by:* J. Markland, A. N. Leather, R. W. Sutton.

Bebbington, Samuel Thomas. British. 14, Tirley Street, Fenton, Stoke-on-Trent. Student, Nottingham University. *Signed by:* D. O. Jordan, T. J. King, F. C. Laxton.

Beck, Harry, M.P.S. British. 17, Exeter Road, London, N.W.2. Pharmacist. *Signed by:* A. Gellman, M. Barent, S. W. Johnson.

***Binks, John Harvey.** British. c/o 52, Deansway, Finchley, N.2. Student. *Signed by:* Alan Maccoll, C. A. Bunton, R. S. Nyholm.

Bird, Marjorie Linda, B.Sc. and Ph.D. (Lond.), F.R.I.C. British. 109, Altenburg Gardens, Clapham Junction, S.W.11. Research Chemist. *Signed by:* Henry Terrey, L. F. Gilbert, E. D. Hughes.

Booth, Roland Gordon, B.Sc. and Ph.D. (Reading). British. c/o Bovril, Ltd., 148/166, Old Street, London, E.C.1. Chief Chemist. *Signed by:* J. King, H. G. Rees, Osman Jones.

***Brown, Archibald Peter,** B.A. (Cantab). British. 7, Pollards Hill West, Norbury, S.W.16. Student. *Signed by:* F. G. Mann, P. Maitland, B. Lythgoe.

Burns, Joseph Lionel, B.A. (Cantab). British. 60, Bulkington Avenue, Worthing, Sussex. Student. *Signed by:* F. G. Mann, P. Maitland, G. W. Kenner.

***Champney, Maurice Anthony.** British. 31, Lindisfarne Road, Wimbledon, S.W.20. Student, Imperial College of Science and Technology, London. *Signed by:* L. S. Theobald, H. N. Rydon, A. A. Eldridge.

***Cleaver, Antony William Thomas,** B.A. (Cantab). British. 56, Ladbrook Road, Solihull, Birmingham. Student. *Signed by:* F. G. Mann, G. W. Kenner, P. Maitland.

Clinch, James. British. 158, Loose Road, Maidstone. Student, Cambridge University. *Signed by:* Alan G. Sharpe, W. G. Palmer, H. J. Emeléus.

Cohen, Gerald, B.Sc. (Illinois). American. 1027, W. Johnson Street, Madison 5, Wisconsin, U.S.A. Student, University of Wisconsin. *Signed by:* Henry J. Schneider, A. L. Wilds, W. S. Johnson.

Cook, Adrian Maxwell, B.Pharm. and Ph.D. (Lond.), Ph.C., A.R.I.C. British. 19, Sidney Road, Beckenham, Kent. Lecturer, School of Pharmacy, University of London. *Signed by:* E. Shotton, L. Saunders, L. K. Sharp, Wilfred H. Linnell.

***Cracknell, John Richard.** British. Brasenose College, Oxford. Chemistry Student. *Signed by:* W. A. Waters, Courtney Phillips, F. M. Brewer.

***Crundwell, Edwin George Barton,** B.A. (Cantab). British. 33, Rowan Road, Bexleyheath. Student. *Signed by:* F. G. Mann, P. Maitland, G. W. Kenner.

***Dawson, Martin Craven,** B.Sc. (Manc.). British. 237, Bolton Road, Salford 6. Research Student. *Signed by:* M. C. Whiting, G. R. Barker, T. G. Halsall.

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Duxbury, Donald, A.R.I.C. British. 23, Lister Street, Accrington. Technical Assistant, Ministry of Supply, Nr. Preston. *Signed by:* David J. Little, Kenneth Shorrock, A. Walton.

England, Brian Daysh, M.Sc. (N.Z.), Ph.D. (Lond.), A.R.I.C. British. Chemistry Department, University College, Ibadan, Nigeria. Lecturer in Chemistry. *Signed by:* R. J. McIlroy, P. B. D. de la Mare, E. D. Hughes.

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Ewence, Joseph Harold, B.Sc. (Lond.), A.R.I.C. British. Santa Elena, Entre Rios, Argentina. Sub-Manager, Meat Works. *Signed by:* J. King, George Taylor, Henry G. Rees.

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Gaimster, Kenneth, B.Sc. (Lond.), A.R.I.C. British. 181, Ardleigh Green Road, Hornchurch. Research Chemist, May & Baker, Ltd. *Signed by:* H. J. Barber, B. J. Heywood, H. J. Cottrell, J. N. Ashley, M. B. Green.

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***Hooton, Kenneth Alan Henry.** British. 4, Catherine Close, Byfleet, Surrey. Laboratory Assistant, Hardingstone Junction Generating Station, Northampton. *Signed by:* D. R. Bell, W. Siddall, D. Gardner.

***Hoyle, Trevor Graham.** British. 34, Mansfield Road, Balby, Doncaster. Assistant Research Chemist. *Signed by:* F. Broomhead, H. Wilson, H. Goddard.

***Jaeckel, Siegfried Michael,** B.Sc. (Lond.), A.R.C.S. British. 6, Arcadia Avenue, Brooklands, Cheshire. Industrial Research Chemist, Petrocarbon Research Laboratory. *Signed by:* H. M. E. Steiner, W. G. Schmidt, E. T. Borrows.

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Jondorf, Werner Robert, B.Sc. (Wales). British. Food Research Station, Lever Bros. and Unilever Ltd., Sharnbrook, Beds. Research Chemist. *Signed by:* H. Ll. Bassett, I. D. Morton, N. M. Cullinane, S. J. Chard.

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***Ley, John Barry.** British. 36, Park Side, Dollis Hill, N.W.2. Student, University College, London. *Signed by:* J. B. Rose, Alan E. Comyns, James E. Gowan.

Liddicoet, Thomas Herbert, B.A. (Coll. of the Pacific, Calif.). American. P.O. Box 646, Diamond Springs, California, U.S.A. Rotary Foundation Fellow, University of Sydney. *Signed by:* R. J. W. Le Fèvre, T. Iredale, Felix Maramba.

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Manly, Thomas David, B.A. (Cantab). British. The Vicarage, Atherstone, Warwickshire. Student. *Signed by:* F. G. Mann, P. Maitland, G. W. Kenner.

***Morrow, David George Dickson,** B.Sc. (Q.U.B.). British. Belfast Bank House, Armagh, Co. Armagh, Northern Ireland. Student. *Signed by:* R. C. Pink, W. W. Hawkins, R. G. R. Bacon.

***Nicholas, Alec Clifford,** B.Sc. (Lond.). British. 46, Wychall Road, Northfield, Birmingham 31. Analytical Chemist, Radiation, Ltd. *Signed by:* J. C. Duff, E. W. Mills, A. R. Roberts.

O'Donoghue, Patrick Noel, B.Sc. (N.U.I.). British. 45, Beulah Road, Thornton Heath. Analytical Chemist, Express Dairy Co. (Caterers), Ltd. *Signed by:* R. Harold Morgan, J. G. Davis, H. Egan.

***Officer, George Arnold.** British. Queen's College, Cambridge. Student. *Signed by:* P. Maitland, B. Lythgoe, V. M. Clark.

***Pajak, Czeslawa.** Polish. 18, Evanston Avenue, London, E.4. Student. *Signed by:* E. Holness, R. W. Jukes, G. Mattock.

***Parsons, Donald Frederick,** B.Sc. (Lond.). British. c/o Imperial College of Science and Technology, Inorganic and Physical Chemistry Department, South Kensington, S.W.7. Post-graduate Student. *Signed by:* J. O'M. Bockris, H. V. A. Briscoe, J. Kenyon.

Patterson, Deryck Stanley Percival, B.Sc. (Lond.). British. c/o 26, Mantan Avenue, Hanwell, W.7. Assistant Chemist. *Signed by:* P. A. Wilkinson, W. Graham, R. J. Nicholls.

***Pizey, James Stephen.** British. 3, Tedworth Square, Chelsea, S.W.3. Student. *Signed by:* A. M. James, D. R. Goddard, J. F. J. Dippy.

***Pocker, Yeshayau,** M.Sc. (Jerusalem). Israeli. 37, Anson Road, 3rd Floor, London, N.7. Chemical Research Student, University College, London. *Signed by:* E. D. Hughes, R. S. Nyholm, R. J. Gillespie.

***Potter, Robert Clive.** British. Connaught Hall, Swaythling, Southampton. University Student. *Signed by:* A. R. Burkin, E. Cartmell, K. R. Webb.

***Pugh, Sylvia Joy.** British. 80, High Street, Solihull Lodge, Warstock, Birmingham 14. Student. *Signed by:* M. L. Tomlinson, E. J. Bowen, R. P. Bell.

Rhodes, William Eric, M.A. (Cantab), A.R.I.C. British. 2, Storey's Way, Cambridge. Technical Manager, Chivers & Sons, Ltd., Histon. *Signed by:* T. P. Hoar, F. H. Banfield, M. Olliver.

***Saxton, Norman Vine.** British. 88, Beresford Avenue, Foleshill, Coventry. Student, The Technical College, Coventry. *Signed by:* Harold Smith, Charles F. Watts, F. S. Brown.

***Simpson, Helen Sophie Davidson.** British. Terchyn, Longtown, Carlisle. Student. *Signed by:* F. G. Mann, B. R. Brown, P. Maitland.

Smart, John Valentine, B.Sc. (Lond.), F.R.I.C. British. 24, Cleveland Road, Barnard Castle, Co. Durham. Chief Analyst. *Signed by:* T. E. V. Horsley, F. C. Bullock, F. W. Anderson.

***Smith, George Boraston,** B.Sc. (L'pool.). British. 85, Prenton Road East, Birkenhead, Cheshire. Research Student. *Signed by:* W. B. Whalley, A. McGookin, David Powell.

Thomas, David Henry, A.R.I.C. British. 13, Liverpool Road, Warrington. Assistant Production Manager. *Signed by:* Arnold Cooksey, Maurice Woodhead, E. Foley.

*__Thompson, Alan Gore,__ B.A. (Cantab). British. Emmanuel College, Cambridge. Student. *Signed by:* F. G. Mann, P. Maitland, B. R. Brown.

*__Trevett, Michael Edwin,__ B.A. (Cantab). British. Lona, Coldharbour, Sherborne, Dorset. Student. (*Signed by:* F. G. Mann, P. Maitland, G. W. Kenner.

__Vischer, Ernst Benedict,__ Ph.D. (Basle). Swiss. Imperial Chemical Industries Ltd., Butterwick Research Laboratories, The Frythe, Welwyn. Research Chemist. *Signed by:* J. Chatt, James S. Moffatt, R. G. Wilkins.

__Wain, Arthur Ernest,__ M.A. (Oxon). British. 6, Kirk Road, Levenshulme, Manchester 19. Research Student. *Signed by:* W. A. Waters, K. W. Bentley, J. A. Alexander.

__Watson, James Stoddart,__ B.Sc. and Ph.D. (Glas.), A.R.I.C. British. Department of Chemistry, National Research Council, Ottawa, Canada. Research Chemist. *Signed by:* Stotherd Mitchell, James Bell, J. C. Speakman.

*__Williams, Derek Farnham,__ B.Sc. (Wales). British. 33, Commercial Street, Ystalyfera, Swansea. Research Student, University College, Swansea. *Signed by:* C. W. Shoppee, D. G. Lewis, E. E. Ayling, R. H. Davies.

UNDER SPECIAL PROVISION APPERTAINING TO CANDIDATES RESIDENT ABROAD.

__Abbas, Syed Mohsin,__ M.Sc. (Delhi). Pakistani. Loughborough College, Loughborough, Leics. Student, Loughborough College. *Signed by:* R. F. Phillips, H. K. Suttle.

__Becker, Ernest I.__ M.S. and Ph.D. (Western Reserve Univ., Cleveland). American. Polytechnic Institute of Brooklyn, 85, Livingston Street, Brooklyn 2, New York, U.S.A. Assistant Professor of Organic Chemistry. *Signed by:* F. M. Beringer.

__Brehm, Warren John,__ A.M. and Ph.D. (Harvard). American. Chemistry Department, New York University, New York 53, New York, U.S.A. Instructor in Chemistry. *Signed by:* Kurt Mislow.

*__Broughton, Frank Jefferson,__ B.Sc. (Trinity Univ. Texas). American. P.O. Box 1525, University Station, Austin, Texas, U.S.A. Student, University of Texas. *Signed by:* Royston M. Roberts.

__Chain, Ernst Boris,__ M.A. and D.Phil. (Oxon), Ph.D. (Cantab), F.R.S. British. Instituto Superiore di Sanita, 299, Viale Regina Margherita, Rome, Italy. Professor of Biochemistry. *Signed by:* S. J. Pirt.

*__Cook, Archibald Stewart,__ B.Sc. (Glas.). British. Rubber Research Institute, P.O. Box 150, Kuala Lumpur, Malaya. Organic Chemist. *Signed by:* A. Walker.

__Davis, Franklin Otto,__ A.B. (Centre Coll. Danville). American. 633, Concord Circle, Trenton 8, New Jersey, U.S.A. Research Chemist, Thiokol Corp. *Signed by:* H. P. Koch.

*__Greene, Frederick D.,__ B.A. (Amherst), A.M. (Harvard). American. Converse Laboratory, Harvard University, Oxford Street, Cambridge 38, Massachusetts, U.S.A. Student. *Signed by:* J. Meinwald, F. Sondheimer.

__Grovenstein, Jr., Erling,__ B.S. (Georgia Institute of Tech.), Ph.D. (Mass. Institute of Tech.). American. Georgia Institute of Technology, School of Chemistry, Atlanta, Georgia, U.S.A. Associate Professor of Chemistry. *Signed by:* Jack Hine.

*__Hill, Richard Keith,__ B.S. (Penn. State Coll.), M.A. (Harvard). American. 20, Wendell Street, Cambridge, Massachusetts, U.S.A. Student. *Signed by:* J. Meinwald.

__Ingersoll, Arthur William,__ M.S. (Nebraska), Ph.D. (Illinois). American. Department of Chemistry, Vanderbilt University, Nashville 4, Tennessee, U.S.A. Professor of Organic Chemistry. *Signed by:* R. L. Evans, Foster D. Snell.

*__Mandell, Leon,__ B.S. (Brooklyn Polytechnic Inst.), M.A. (Harvard). American. 10, Brockton Street, Mattapan, Massachusetts, U.S.A. Student. *Signed by:* Joseph Jordan.

__Mehkari, Md. Asadullah,__ B.Sc. (Karachi). Pakistani. 58/4, Shikarpur Colony, Karachi 5, Pakistan. Chief Chemist and Bacteriologist, Pakistan Pharmaceutical Laboratories. *Signed by:* R. A. Khan.

__Milde, Roy Leander,__ M.S. (N. Dakota State Coll.), Ph.D. (Purdue). American. 810, Lake Park Drive, Baton Rouge, Louisiana, U.S.A. Research Chemist and Assistant Manager, Ethyl Corp. *Signed by:* Henry M. Hellman.

*__Muetterties, Earl Leonard,__ B.S. (Northwestern), M.S. (Harvard). American. 20, Wendell Street, Cambridge, Massachusetts, U.S.A. Student and Teaching Fellow, Harvard University. *Signed by:* John T. Rundquist.

__Munasinghe, Don Chandrasena,__ B.Sc. (Lond.). Ceylonese. No. 12, School Lane, Wellawatta, Colombo, Ceylon. Assistant Chemist, Department of Industries. *Signed by:* M. U. S. Sultanbawa, A. Sundralingham.

__Phillips, Arthur Page,__ M.S. (Tufts Coll. Mass.), Ph.D. (N.Y.). American. 2542, University Avenue, Bronx, New York 63, New York, U.S.A. Research Organic Chemist. *Signed by:* P. B. Russell.

__Rapoport, Henry,__ Ph.D. (Mass. Inst. of Tech.). American. Chemistry Department, University of California, Berkeley 4, California, U.S.A. Assistant Professor. *Signed by:* Donald S. Noyce.

__Roux, David Gerhardus,__ M.Sc. (S.A.). South African. Leather Industries Research Institute, Rhodes University College, Grahamstown, Cape Province, South Africa. Organic Research Chemist. *Signed by:* W. F. Barker.

__Sen, Binayendra Nath,__ M.Sc. (Calcutta). Indian. Mithapukur, Burdwan, West Bengal, India. Professor of Chemistry, Calcutta University. *Signed by:* G. K. Mukherjee.

Seyb, Leslie Philip, M.S. and Ph.D. (Iowa). American. Research Laboratory, Diamond Alkali Co., Painesville, Ohio, U.S.A. Manager of Research. *Signed by:* Ralph L. Evans, Foster D. Snell.

Shapiro, George Bernard, B.S. (Polytechnic Inst. of Brooklyn). American. 18, Schermerhorn Street, Brooklyn 2, New York, U.S.A. Instructor in Chemistry. *Signed by:* F. M. Beringer.

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PAPERS RECEIVED.

(List of papers received between November 18th and December 8th, 1950.)

"Attempts to prepare new aromatic systems. Part III. *cyclo*Pentindene." By WILSON BAKER and P. G. JONES.

"Characteristic absorption bands, in the 10-μ. region, of the infra-red spectra of *cyclo*-paraffin derivatives." By L. W. MARRISON.

"A new reagent for the oxidation of acyloins to diketones." By W. RIGBY.

"The nuclear chlorination of toluene: 2 : 3 : 4- and 2 : 3 : 6-trichlorotoluene." By H. C. BRIMELOW, R. L. JONES, and T. P. METCALFE.

"The nature of the co-ordinate link. Part II. Halogen-bridged, binuclear platinous complexes; the co-ordination affinity of the tertiary alkyls of Group V elements for platinous chloride." By J. CHATT.

"A contribution to the chemistry of the carbazoles. 1 : 2 : 3 : 4-Tetrahydro-4-ketocarbazoles." By G. R. CLEMO and D. G. I. FELTON.

"The influence of structure on the ultra-violet absorption spectra of heterocyclic systems." By G. R. CLEMO and D. G. I. FELTON.

"Some oxidation–reduction reactions of hydroxylamine." By P. DAVIS, M. G. EVANS, and W. C. E. HIGGINSON.

"Quaternary ammonium salts. Part II. A comparison between the effect of the carbonyl and the ethylene group on the decomposition of the quaternary ammonium radicals." By W. TADROS and A. LATIF.

"Quaternary ammonium salts. Part III. Synthetic œstrogens related to triphenylethylene. Part III. Decomposition of some quaternary ammonium salts of triphenylethylene." By W. TADROS and A. LATIF.

"The chemistry of extractives from hardwoods. Part IV. Okanin and *iso*okanin, the isomeric 2 : 3 : 4 : 3′ : 4′-pentahydroxychalkones." By F. E. KING and T. J. KING.

"The structure of β-cyperone." By F. J. MCQUILLIN.

"The characteristic infra-red frequencies of the carboxylic acid group." By M. ST. C. FLETT.

"Experiments on the preparation of indolocarbazoles. Part IV. The preparation of indolo(2′ : 3′-2 : 1)carbazole." By M. L. TOMLINSON.

"Interaction of alcohols and silicon tetrachloride." By W. GERRARD and A. H. WOODHEAD.

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"Coumariloyl peroxide and its decomposition in organic solvents." By M. C. FORD and W. A. WATERS.

"The structure of the dinitrososulphite and the sulphamate ion." By G. A. JEFFREY and H. P. STADLER.

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"The enzymic synthesis and degradation of starch. Part XII. The mechanism of synthesis of amylopectin." By P. N. HOBSON, W. J. Whelan, and S. Peat.

"Deoxy-sugars. Part XIV. A further contribution to the chemistry of 2-deoxy-D-galactose." By A. B. FOSTER, W. G. OVEREND, and M. STACEY.

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ANNUAL REPORTS ON THE PROGRESS ON CHEMISTRY FOR 1949

Volume XLVI **Published July, 1950**

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